(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 October 2001 (04.10.2001)

PCT

(10) International Publication Number
WO 01/73444 A2

(51) International Patent Classification[7]: G01N 33/68, C07K 14/00, G06F 19/00

(21) International Application Number: PCT/GB01/01358

(22) International Filing Date: 27 March 2001 (27.03.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/192,180 28 March 2000 (28.03.2000) US

(71) Applicant *(for all designated States except US)*: **CAMBRIDGE UNIVERSITY TECHNICAL SERVICES LIMITED** [GB/GB]; The Old Schools, Cambridge, Cambridgeshire CB2 1TS (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **FARNDALE, Richard, William** [GB/GB]; 21 Hawthorne Road, Stapleford, Cambridge, Cambridgeshire CB2 5DU (GB). **EMSLEY, Jonas** [GB/GB]; Flat 1, 169A London Road, Leicester, Leicestershire LE2 1EG (GB). **KNIGHT, Clive, Graham** [GB/GB]; 238 Queen Edith's Way, Cambridge, Cambridgeshire CB1 8NL (GB). **BARNES, Michael, John** [GB/GB]; 229 Chesterton Road, Cambridge, Cambridgeshire CB4 1AN (GB). **LIDDINGTON, Robert, Colin** [GB/US]; The Burnham Institute, 10901 North Torrey Pines Road, La Jolla, CA 92037 (US).

(74) Agents: **WALTON, Sean, M.** et al.; Mewburn Ellis, York House, 23 Kingsway, London, Greater London WC2B 6HP (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

AA

WO 01/73444 A2

(54) Title: RECEPTOR/PEPTIDE CRYSTAL STRUCTURE FOR IDENTIFICATION OF INHIBITORS

(57) Abstract: The crystal structure of a collagen peptide in complex with integrin α2 I-domain is provided. Coordinates for the crystal structure are useful in designing novel molecules that can be tested for binding to the receptor and other I-domains and preferably ability to inhibit I-domain binding to ligand, and I-domain function. Regions of I-domains that undergo conformation change upon ligand binding are also identified and provided as targets for binding molecules such as antibodies. Molecules that inhibit the function of polypeptides comprising I-domains are of therapeutic potential in a number of diseases and disorders.

RECEPTOR/PEPTIDE CRYSTAL STRUCTURE FOR IDENTIFICATION OF INHIBITORS

Technical Field

The present invention relates to use of coordinates of peptide/receptor crystal structure in designing and obtaining molecules that inhibit protein I-domain interactions and function, especially collagen/receptor interaction, and are of therapeutic potential. The present invention relates to modulating platelet aggregation, adhesion and activation, as well as the adhesion, migration and phenotypic expression of many other cells, and inhibitors of collagen interaction with collagen receptors.

Background Art

Collagens and collagen-related peptides

The collagens provide the vertebrate organism with tensile strength; they are the major protein component of skin, bone, cartilage and other connective tissue. Collagens, for example Type IV, provide a network of protein known as the basal lamina to which cells can attach and over which cells can migrate. Such structures are found beneath endothelial and epithelial cell layers in many locations. Deeper into tissues such as the epidermis or the intimal layer of the blood vessels, fibrous collagens such as Types I and III are found [2]. The structure and precise amino acid composition of the collagens varies with type. Each type is the product of a distinct gene or genes. What characterises a protein as a collagen is that it contains, substantially or in some part, a triple-helical structure in which three polypeptide chains, each helical in its own right, are wound around one another to

form a superhelix. A specific amino acid sequence, Gly-Pro-Hyp, (GPO in single-letter nomenclature) when repeated sufficiently can support triple-helical conformation. A related sequence, GPP, also adopts a triple-helical conformation.

The properties of these sequences which support triple-helical structure are:
(i) the tight bends associated with the strained ring structure of the iminoacids proline and hydroxyproline,
(ii) the presence of glycine at every third residue whose side chain, simply a hydrogen atom, positioned in the interior of the cylinder defined by the triple helix, is so small as to present no obstacle to the protein chains associating in this conformation, and
(iii) the capacity of the hydroxyproline residues in particular to support intra- or inter-chain hydrogen bonding, thus stabilising the helix.

In long peptides, where such effects may be additive over many triplets of amino acids, substantial deviation from the GPO prototypic sequence still allows triple-helical structure. Thus, in Type I collagen, where the explicit triplet GPO comprises only around 10% of the primary sequence of the molecule, which is over three hundred triplets in length, the structure exhibits a melting temperature, i.e. the temperature at which the helix will unwind, in excess of 40°C, significantly higher than physiological temperatures. In nature, the helix and its higher order assembly, the collagen fibril, is further stabilised by cross-linking.

Synthetic peptides are known where, utilising a sequence of repeating GPP triplets or repeating GPO triplets,

significantly higher melting temperatures can be achieved. For example, peptides comprising $[GPO]_{10}$ melt at about 60°C [3], but $[GPO]_5$ melts at below 20°C [4-6].

Such synthetic peptides have found increasing application in biomedical research, since they may have biological activity. For example, in cross-linked form the sequence $[GPO]_{10}$ will bind to a specific platelet receptor population, known as glycoprotein VI, on human platelets and activate them, most likely by stabilising these receptors in close proximity, allowing proteins associated with their intracellular domains to interact [7-10]. Clustering of receptors in this way may be one mechanism by which signals, such as a change in phosphorylation state of intracellular proteins, may propagate within the platelet [10, 11]. This mechanism is thought to be a key activatory step in haemostatic events leading to platelet aggregation, and in pathological events including thrombosis [12-14]. Thus the peptide containing the GPO motif, known as collagen-related peptide or CRP, provides a receptor-specific peptide useful in the study of platelet activation [8].

Peptide motifs which support triple helical structure, i.e. GPO or GPP, can be used as flanking sequences which confer triple-helical structure upon other sequences from collagen, or indeed from other proteins, which would not otherwise adopt this conformation [15-18]. Such peptides allow the researcher to investigate the properties of small sequences from the primary structure of the collagen alpha chains, such as the alpha 1 chain from type I collagen, or the alpha 2 chain from type I collagen or the alpha 1 chains of type III collagen, whilst retaining the triple-helical structure which is crucial for cell-reactivity. Such investigations have allowed other

specific receptor-binding sequences to be identified.

One such is the sequence GFOGER, which binds to a further class of receptors, the integrins α1β1 and α2β1 [18].

The integrins

The integrins are expressed on the surface of cells, being widespread throughout the different tissues of the body, and their functions are manifold. Integrins are heterodimeric structures, comprising two subunits, designated α and β [19] Certain combinations of the 20 or so known α subunits with the 10 or so known β subunits are allowed, whilst many are excluded and do not occur in nature. Thus, at present, about 30 different integrins are known in man. Their selectivity for particular ligands derives primarily from the combination of subunits, but may be dependent also upon the activation state of the integrin [20, 21].

Some integrins mediate direct cell-cell contact, as between leukocytes, or between the cells forming a cell layer or epithelium. Often, counter-receptors such as the cellular adhesion molecules (CAMS) may bind to such integrins [22]. This represents the model by which the β2 integrins found upon the leukocyte surface mediate cell-cell contact. Commonly, integrins are found to bind to extracellular proteins of the plasma (such as fibrinogen) or of the matrix (such as collagen or fibronectin). Very often, the amino acid sequences supporting interaction with integrins include an acidic residue such as D or E. Thus the sequence RGD can bind to the fibrinogen receptor, αIIbβ3, the vitronectin receptor αvβ3, to the fibronectin receptor, α5β1 and to certain other integrins [20]. Sequences elsewhere within the ligand may enhance and

provide further selectivity to this primary interaction.

Integrin α subunits can be described as having a modular structure, with seven consensus repeats in their extracellular domains [23]. Some of these, known as EF-hands, bind cations, Ca^{2+}, for example, (although other divalent cations such as Zn^{2+}, Co^{2+} or Mn^{2+} may serve the same purpose) which support the activity of the receptor. One property of the αIIb subunit of the fibrinogen receptor known to depend upon the presence of these divalent cations is the ability to associate with the β3 subunit, essential for receptor function [24].

Integrin α subunits fall into two classes, those as described above and those which possess an additional protein module, the inserted domain or I-domain, which is sometimes known as the A-domain because it adopts the same fold and may share other properties with the A-domains of the protein, von Willebrand factor.

The collagen-binding integrins, α1β1 and α2β1 contain I-domains [25]. These I-domains are crucial for the capacity of the integrin to bind collagen, which resides in a characteristic structure at one end of the domain which binds a divalent cation. Several species of cation can occupy this site, for example Mg^{2+} or Co^{2+} or Mn^{2+} [26]. In physiology it is likely that Mg^{2+} may be the ion present in this specialised binding structure, known as the metal ion dependent adhesion site or MIDAS. Because of its crucial role in mediating collagen binding, the I-domain MIDAS is the subject of close scrutiny in the field.

Protein domains are defined as stretches of sequence which

fold independently into the native conformation of the peptide, i.e. when separated from other regions of the parent protein. The I-domain, in suitably pure form, expressed, for example as a recombinant protein, can re-fold [26] into a structure which has the same capacity to bind cations in its MIDAS and the same capacity to bind ligands as the parent integrin [27]. For this reason, the α2 I-domain provides a ready model for studying the interaction of collagen with α2β1.

A key question has been how the binding of ligand to the I-domain may alter its structure, which various techniques have been applied to address. For example, suitable computer algorithms allow fold prediction to be made, based upon the known primary sequence and by analogy with other I-domains or A-domains, which may provide an important input to this process. Such algorithms might allow a proposed ligand-binding cleft to be visualised in 3-dimensions, and to be compared with the known shape of the ligand. Often, suitable algorithms provide an analysis of the charge density on the surface of both the ligand and the proposed binding cleft, to establish complementary sites which might provide the basis for their interaction.

Previous work has elucidated the structure of the α2 I-domain in its free, unligated form [26]. The key feature of I domains and vWf A-domains is that they contain a characteristic assembly of five parallel and one anti-parallel beta-strands which form the stable platform of the structure. This conformation, known as the dinucleotide-binding fold (or Rossman fold) is found in other proteins such as NAD hydrolase, guanine nucleotide-binding proteins and protein kinases. Common to all of these structures is that ligand

binding occurs at the C-terminal surface formed by these beta-strands, although this has not hitherto been formally demonstrated. So it is with the integrin I-domains. This structure is linked by a series of peptide loops, several of which elaborate α-helices and at least one anti-parallel beta strand which substantially enclose the beta-sheet as they return to the base of the beta-sheet structure.

Another crucial feature of I-domains is that they possess an amino acid motif regarded as diagnostic of I-domains, having the sequence DxSxS, where x may represent any amino acid. These three amino acids, D151, S153 and S155, are present in the N-terminal loop arising from the first beta strand of the α2 I-domain. These, along with other oxygen-containing residues in nearby peptide loops, co-ordinate the metal ion and constitute the MIDAS.

In the case of α2 I-domain, beta-strand 5 elaborates above it a single turn of α-helix, known as the C-helix. A C-helix is known to exist in the α1 I-domain, and might be predicted in other, less well-characterised I-domains. This appears to obstruct the MIDAS in its un-ligated state. It seems very likely that similar structures may occur in other I-domains.

Structure determination

Structure prediction, based upon the primary sequence of a protein domain, although a useful adjunct to the research endeavour, needs to be confirmed by measurement. The procedures used for such purposes include nuclear magnetic resonance and X-ray crystallography. Each approach offers its own advantage: nuclear magnetic resonance allows the examination of proteins in aqueous media, and at temperatures

close to physiological. However, nuclear magnetic resonance requires that the proteins be synthesised during their expression from amino acids comprising atomic nuclei with unpaired spin, such as ^{15}N or ^{13}C, in their peptide or other bonds. Protons within the structure may need to be replaced by deuterons which do not resonate. This may present a significant difficulty, especially given that quite high protein concentration, such as 1 millimolar, and volume, such as 1 millilitre, may be needed to allow the analysis to proceed. Further, the magnetic resonance are critically-dependent upon the size of the target protein, so that structures larger than about 100 amino acids are difficult to obtain, because of limitations of the field strength and frequency of the instrument.

X-ray diffraction also suffers from practical constraints, the major drawback being that the protein under examination must crystallise under laboratory conditions to provide a crystal of sufficient size and homogeneity as to be useful for subsequent analysis. Suitable instruments include quite widespread laboratory-scale X-ray diffraction units, useful in the initial examination of the crystal, or the much larger-scale synchrotron devices. The choice of instrument is governed by the size of the crystal available and the spatial resolution required of the analysis.

In the crystallisation of two structures as a complex, further constraints emerge. Firstly, the complex must adopt an appropriate, presumably physiological, conformation. Secondly, the association between the two species must be stable at solution temperatures. Thirdly, the dimensions of the complex must be such as to allow unit cells, i.e. the most fundamental level of organisation of the complex, to align in

an array which can form a crystal. Where the two species are of grossly different shapes or sizes, this may be a meaningful constraint. For example, the tropocollagen molecule, the triple helical structure comprising the intact α-chains of the collagen in question, may approximate to a rod about 300nm in length, whereas the I-domain of the integrin α2β1 approximates to a sphere about 3nm diameter. It is unlikely that a complex formed from single copies of such disparate structures will crystallise, although complex formation might very well occur.

Disclosure of the Invention

The present invention is based on work in which a collagen peptide was produced as a trimer, and a crystal structure obtained for the complex formed by binding of the peptide to integrin α2 I-domain. Coordinates for the crystal structure are useful in designing novel molecules that can be tested for binding to the receptor and other I-domains, and preferably ability to inhibit I-domain binding to ligand (e.g. collagen) and function. Regions of I-domains that undergo conformational change upon ligand binding are also identified and provided as targets for binding molecules such as antibodies. Molecules that inhibit the function of polypeptides comprising I-domains are of therapeutic potential in a number of diseases and disorders. The coordinates of the crystal structure for use in aspects and embodiments of the present invention are shown in Table 1. Specific contacts of additional interest are shown in Table 2. Details of interaction between peptide and receptor are shown in the Figures, described below.

The coordinates of Table 1 provide a measure of atomic location in Angstroms. The coordinates are a relative set of

positions that define a shape in three dimensions. The skilled person would recognise that it is possible that an entirely different set of coordinates having a different origin and/or axes could define a similar or identical shape. Furthermore, he would recognise that varying the relative atomic positions of the atoms of the structure so that the root mean square deviation of residue backbone atoms (i.e. the nitrogen-carbon-carbon backbone atoms of protein amino acid residues) is less than 1.5 Å (preferably less than 1.0 Å and more preferably less than 0.5 Å) when superimposed on the coordinates provided in Table 1 for the residue backbone atoms, will generally result in a structure which is substantially the same as the structure of Table 1 in terms of both its structural characteristics and potency for structure-based drug design. Likewise he would recognise that changing the number and/or positions of the water molecules of Table 1 will not generally affect the potency of the structure for structure-based drug design of I-domain inhibitors. Thus for the purposes described herein as being aspects of the present invention, it is optionally within the scope of the invention if: the Table 1 coordinates are transposed to a different origin and/or axes; the relative atomic positions of the atoms of the structure are varied so that the root mean square deviation of residue backbone atoms is less than 1.5 Å (preferably less than 1.0 Å and more preferably less than 0.5 Å) when superimposed on the coordinates provided in Table 1 for the residue backbone atoms; and/or the number and/or positions of water molecules is varied. Reference herein to the coordinates of Table 1 thus optionally includes the coordinates in which one or more individual values of Table 1 are varied in this way.

Also, the skilled person would recognise that modifications in

the α2 I-domain crystal structure due to e.g. mutations, additions, substitutions, and/or deletions of amino acid residues could account for variations in the atomic coordinates of the complex. Therefore, atomic coordinate data of the α2 I-domain modified so that a ligand that bound to the α2 I-domain would also be expected to bind to the modified α2 I-domain are, for the purposes described herein as being aspects of the present invention, optionally also within the scope of the invention. Reference herein to the coordinates of Table 1 thus optionally includes the coordinates modified in this way.

Furthermore, the Table 2 coordinates being derived from Table 1, reference herein to the coordinates of Table 2 optionally includes the coordinates in which one or more individual values of Table 2 are changed as a result of the above-mentioned variation and/or modification of the coordinates of Table 1.

The crystal structure defined by the co-ordinates may be visualised and rendered by many molecular graphics programmes, suitable examples of which include MolView (T.J. Smith, Dept. Biology, Purdue University, In47907, USA), RasMol Molecular Graphics (Roger Sayle, Biomolecular Structures Group, Glaxo Wellcome Research & Development, Stevenage, Hertfordshire, UK), Swiss PDB Viewer (Glaxo Wellcome Experimental Research) or XtalView (D.J. McRee, (1992) J. Mol. Graphics, 10, 44-47). Many other software suites are available to the skilled researcher.

Modelling and refinement of crystallographic data can be performed using AMORE [30] and XtalView, or other suitable software, as noted in the Methods section below.

The use in rational drug design of both the co-ordinates produced by these algorithms and the identity and chemical nature of the atoms involved in the interaction between I-domain and ligand, presented in Table 2, may involve use of interpretive software such as MCSS (Miranker, A. and Karplus, M., "Functionality Maps of Binding Sites: a Multiple Copy Simultaneous Search Method," Proteins: Structure, Function, and Genetics, 11 29-34 (1991)).

Use of these data in identification of chemical compounds which may be potential ligands or inhibitors of the I-domain:collagen interaction may utilise database searching software such as HOOK: A Program for finding novel molecular architectures that satisfy the chemical and steric requirements of a macromolecule binding site, (Eisen, M. B., et al., Proteins, 19 199-221 (1994)) or DOCK (Meng, E.C. et al., J. Comput. Chem. 13, 505-524 (1992)). Suitable databases of candidate ligands may include the ACD (Available Chemicals Directory; Molecular Design Limited Information Systems, San Leandro, CA, USA) or the NCI Drug Information System 3D Database (National Cancer Institute, USA).

A binding motif within collagen was previously identified, the sequence GFOGER [17, 18]. As for the parent molecule, this amino acid sequence adopts a triple helical conformation, when flanked by suitable repeats of GPO or GPP triplets, and binds to the integrin. Evidence for this is provided by the observation that the sequence is inactive when flanked by repetitive GAP motifs [18], so that non-helical structure is adopted, rather than the GPP or GPO motifs described above which support triple-helical conformation.

The structure of the candidate peptide is determined by the various requirements for co-crystallisation. If the flanking sequences of GPP or GPO are too long, then the dimensions of the triple-helix no longer match those of the I-domain, and crystallisation will be increasingly less likely, as outlined above. But it remains important that sufficiently long flanking sequences are present to maintain triple-helical structure even at the cold-room temperature (0-8EC, typically 4EC) used for crystallisation. Hence the extent of the flanking triplets is likely to be critical, being long enough to support triple-helical structure but not so long as to impede crystallisation.

A further consideration is that the peptide should be located centrally upon the I-domain, so that the complex is approximately symmetric, a property which favours crystallisation.

In accordance with the present invention, a peptide has been synthesized comprising $[GPO]_2GFOGER[GPO]_3$ which has a melting temperature of about 22°C and allows co- crystallisation to proceed at cold-room temperatures, where 95% or more of the peptide is in triple-helical form (see Figure 1). This peptide forms a single turn of the triple-helix after assembly in trimer. Further, the disposition of two GPO triplets at the N-terminus of the peptide and three at the C-terminus allows the crucial glutamate (E) residue to be centrally located within the resultant triple-helix, favouring a symmetrical complex with the α2 I-domain.

An important consideration in the design of this peptide is the chemical modification of charged groups at its amino-

terminus and carboxy-terminus. This has the effect of rendering the ends of the peptide neutral at physiological pH, so that electrostatic repulsion between adjacent chains within a triple-helix is minimised. This permits the peptide to assemble as a triple-helix at higher temperature, so facilitating the use of shorter peptide ligands, consistent with the dimensions of the receptor, in the crystallisation process. Several chemistries may be suitable. In the present case, acetylation of the N-terminal amino group and incorporation of a C-terminal amide achieved this purpose.

Methods useful in attempts to induce crystallisation are known in the art [28]. Crucial factors may be the inclusion of suitable buffers to maintain the appropriate charge of the protein and the peptide ligand; suitable detergents to maintain the conformation of the receptor; suitable polymers to increase the effective concentration of both receptor and ligand; suitable concentration of divalent cation to saturate the MIDAS; suitable concentration of peptide; precipitants to induce the gradual precipitation/crystallisation of the complex; that the crystallisation be performed at temperatures at which the peptide is triple-helical; glycerol to stabilize the I domain and act as a cryo-protectant during the flash freezing prior to data collection.

Once the crystallisation and X-ray diffraction data have been obtained, then the 3-dimensional co-ordinates of the atoms within the crystal may be deduced by the use of suitable computer algorithms. The resultant data set allows the construction of 3-dimensional models of the ligand in complex with the receptor, which offers to the researcher a fundamental understanding of the interaction between the two.

Knowledge of the structure of the ligand-I domain complex allows key processes to be established, such as a change in conformation in the receptor or ligand as the complex forms. Such information allows for the design of materials which interact with the receptor, most likely at the site of interaction, the MIDAS, but possibly elsewhere in the structure, for example in the C-Helix or near Helix α7. Such materials may be used to impede the activation process of the integrin, preventing collagen from binding to the receptor. In therapeutic use, such materials may be used to prevent cell contact with collagen, so impeding disease processes such as thrombosis, atherogenesis and metastasis.

In general aspects, the present invention is concerned with identifying or obtaining potential inhibitors of Integrin I-domain interaction with ligand (e.g. collagen) and/or function, and in preferred embodiments identifying or obtaining actual inhibitors of such interaction and/or function. Crystal structure information presented herein is useful in designing potential inhibitors and modelling them or their potential interaction with the I-domain of Integrin α2β1 or other I-domain. Potential inhibitors may be synthesized and brought into contact with the relevant I-domain to test for ability to interact with the I-domain, ability to inhibit interaction of the I-domain with collagen or other ligand, or with a collagen peptide that binds the I-domain, and/or ability to affect I-domain or Integrin function. Actual inhibitors may be identified from among potential inhibitors synthesized following design and model work performed *in silico*. An inhibitor identified using the present invention may be formulated into a composition, for instance a composition comprising a pharmaceutically acceptable excipient, and may be used in manufacture of a medicament for

use in a method of treatment. These and other aspects and embodiments of the present invention are discussed below.

Table 2 provides details of contacts between the peptides and I-domain in the crystal structure. These too may be used in design of molecules that make similar contacts with the I-domain. Such molecules may be synthesised and tested for ability to interact with the I-domain, ability to inhibit interaction of the I-domain with collagen or with a collagen peptide that binds the I-domain, and/or ability to affect I-domain or Integrin function.

Comparison of the structure of the I-domain crystallised with the triple-helical peptide and the I-domain crystal structure without the peptide identifies a number of changes in conformation in the I-domain on peptide binding, and consequently parts of the I-domain which may be targeted for inhibition. This is discussed further below.

In accordance with a first aspect of the present invention there is provided a method of identifying a potential inhibitor of an I-domain-containing polypeptide, especially an integrin I-domain, e.g. selected from the group consisting of α1, α2, α10, α11, αD, αE, αL, αM and αX, preferably α2 or α1 and most preferably α2, the method comprising either (i) employing a three-dimensional structure of the Integrin α2 I-domain as shown in Table 1 to design or select a potential inhibitor, (ii) designing or selecting a potential inhibitor that interacts with one or more points in the I-domain crystal structure shown for the I-domain in Table 2, or (iii) designing or selecting a potential inhibitor that mimics one or more (and preferably three or more) points in the peptide structure shown for the peptide structure in Table 2.

In accordance with a further aspect of the present invention there is provided a method of identifying a potential inhibitor of an I-domain-containing polypeptide, especially an integrin I-domain, e.g. selected from the group consisting of α1, α2, α10, α11, αD, αE, αL, αM and αX, preferably α2 or α1 and most preferably α2, the method comprising the steps of:

(a) employing a three-dimensional structure of the Integrin α2 I-domain as shown in Table 1 to design or select a potential inhibitor;

(b) synthesizing or providing said potential inhibitor; and

(c) testing said potential inhibitor for ability to interact with an I-domain-containing polypeptide.

A potential inhibitor of an integrin or other I-domain containing polypeptide may be designed by modelling points of interaction between the trimerized collagen peptide and the α2β1 I-domain, for example as shown in Table 2. One or more electrostatic interactions and/or one or more hydrogen bonds and/or one or more hydrophobic interactions may be used in the modelling. In a preferred embodiment, all the I-domain points identified in Table 2 are employed in the design, and/or all the peptide points identified in Table 2.

Thus, in a further aspect the present invention provides a method of identifying a potential inhibitor of an I-domain-containing polypeptide, especially an integrin I-domain, e.g. selected from the group consisting of α1, α2, α10, α11, αD, αE, αL, αM and αX, preferably α2 or α1 and most preferably α2, the method comprising the steps of:

(a) designing or selecting a potential inhibitor that

interacts with one or more points in the I-domain crystal structure shown for the I-domain in Table 2;

(b) synthesizing or providing said potential inhibitor; and

(c) testing said potential inhibitor for ability to interact with an I-domain-containing polypeptide.

In a further aspect the present invention provides a method of identifying a potential inhibitor of an I-domain-containing polypeptide, especially an integrin I-domain, e.g. selected from the group consisting of α1, α2, α10, α11, αD, αE, αL, αM and αX, preferably α2 or α1 and most preferably α2, the method comprising the steps of:

(a) designing or selecting a potential inhibitor that mimics one or more points in the peptide structure shown for the peptide structure in Table 2;

(b) synthesizing or providing said potential inhibitor; and

(c) testing said potential inhibitor for ability to interact with an I-domain-containing polypeptide. Preferably, in step (a) the potential inhibitor mimics three or more spaced points in the peptide structure.

Step (c) of each of the above aspects may comprise bringing said potential inhibitor into contact with the I-domain-containing polypeptide to determine ability of said potential inhibitor to inhibit (i) ability of the I-domain to interact with collagen or a collagen peptide or other ligand which binds the I-domain, and/or (ii) I-domain or I-domain-containing polypeptide function. The I-domain-containing polypeptide may be an integrin (e.g α2β1).

Integrin function may be measured in a number of different

ways.

For instance, cells which express the integrin may be allowed to come into contact with a surface coated with a substrate known to bind the integrin. By illustration with reference to α2β1 Integrin as a preferred embodiment without limitation to the ability to employ other integrins and I-domains in embodiments of the present invention, cells, such as human or other platelets, or any cell type utilising α2β1 as an adhesive receptor, or cells such as HT1080 cells which use only α2β1 as a receptor for collagen, may be allowed to settle upon the surface, and after suitable incubation time, e.g. from 10 minutes to 1 hour, or to 3 hours or longer, be washed from the surface [18]. Cells removed by this washing procedure may be quantitated, for example using an electronic particle counter [18], a haemocytometer, or other suitable procedure, allowing the proportion of cells that is not removed by washing to be defined as adherent. Alternatively, such cells as remain, constituting adherent cells, may be quantitated directly, either by microscopical counting, or if radiolabelled cells were used, then the amount of radioactivity remaining may be measured, or the cells may be stained using histochemical dyes and the amount of stain retained may be quantitated colorimetrically, or cells may be lysed using suitable detergent or other procedure, and the enzymes released from the cells may then be quantitated colorimetrically as a measure of the adherent cell numbers [18]. Each of these, or other suitable procedure, allows the adhesion of cells via α2β1 to be measured, which defines the function of the integrin. Such procedures are well-known to those skilled in the art [refs 3,7,16,17,18,25,27].

In another variant of the procedure, similar surfaces coated

with substrate, such as peptide or collagen as defined above, may be used to support the adhesion of the purified integrin $\alpha 2\beta 1$ or of the recombinant $\alpha 2$ I-domain. In these variants, the receptor or I-domain is suitably labelled, for example with biotin [18], or, if expressed as recombinant fusion protein, with a poly-His tag, or glutathione-S-transferase, or with a fluorescent dye or with any other suitable means of identification, each of which may readily be detected by routine methodology. Alternatively, the protein may be allowed to interact directly with a specific antibody, and its presence may then be detected immunologically. Such assays allow the extent to which the integrin or I-domain adheres to the substrate to be determined, which is a measure of integrin function.

Alternatively or additionally, step (c) of the above aspects may comprise the sub-steps of:

(i) forming a complex of the I-domain-containing polypeptide and said potential inhibitor ; and

(ii) analysing said complex by X-ray crystallography or NMR spectroscopy to determine the ability of said potential inhibitor to interact with the I-domain-containing polypeptide. Detailed structural information can then be obtained about the binding of the potential inhibitor to the I-domain-containing polypeptide, and in the light of this information adjustments can be made to the structure or functionality of the potential inhibitor, e.g. to improve binding to the polypeptide.

A further aspect of the present invention (which may be used in the above-mentioned analysis sub-step (ii)) provides a method of analysing an I-domain-containing polypeptide complex comprising employing (i) X-ray crystallographic diffraction

data from the I-domain-containing polypeptide complex and (ii) atomic coordinate data according to Table 1 to generate a difference Fourier electron density map of the complex.

Therefore, an I-domain-containing polypeptide complex can be crystallised and analysed using X-ray diffraction methods, and a difference Fourier electron density map can be calculated based on the X-ray diffraction pattern of the complex and the solved structure for the I-domain of Table 1. Such a map can be used to determine whether and where a particular ligand binds to the I-domain and/or changes to the conformation of the I-domain.

Electron density maps can be calculated using programs such as those from the CCP4 computing package (Collaborative Computational Project 4. The CCP4 Suite: Programs for Protein Crystallography, Acta Crystallographica, D50 760-763, (1994)). For map visualisation and model building programs such as O (Jones et al., Acta Crystallographica, A47 110-119 (1991)). Structure factor data, which are derivable from atomic coordinate data (see e.g. Blundell et al., in *Protein Crystallography*, Academic Press, New York, London and San Francisco, (1976)), are particularly useful for calculating difference Fourier electron density maps.

Analysis of the changes in conformation of the α2 I-domain allows certain residues to be identified as becoming exposed upon ligand binding: residues E318 (at the N-terminal end of Helix α7) and D292 (close to the N-terminal end of Helix α6). Inhibitors of the I-domain and integrin function may be identified by targeting a binding molecule to the regions of the I-domain including these amino acids, for example by generating antibodies or other binding molecules to sequences

comprising, for instance residues 315 to 320, or 288 to 295. Certain parts of the I-domain, for example the C-helix, residues 284 to 288, also dramatically alter their conformation upon binding. These similarly provide a target to inhibit conformational change, with therapeutic potential.

Thus, in a further aspect the present invention provides a method of obtaining a potential inhibitor of an Integrin, the method comprising the steps of:

(a) providing a peptide fragment of Integrin α2 I-domain, which peptide fragment contains the E318 residue (e.g. comprises residues 315-320), the D292 residue (e.g. comprises residues 288-295)or the residues 284-288;

(b) bringing the peptide fragment into contact with a test substance, such as an antibody molecule; and

(c) determining the ability of the peptide fragment to bind with the test substance.

A substance which binds the peptide, e.g. an antibody molecule, is a potential inhibitor of integrin function, e.g. Integrin α2β1 function. Ability of a potential inhibitor actually to inhibit may be determined as discussed elsewhere herein.

Similarly, the present invention provides for identifying a molecule that interacts with any part of the integrin I-domain identified by means of the crystal structure disclosed herein as making a contact with another part of the I-domain or the peptide in the crystal, or as altering in conformation on binding of the peptide.

Data presented in Table 1 allows identification of those residues and their corresponding co-ordinates within the

resting I-domain (Brookhaven Protein Database number 1aox, reference 26) which are critically involved in both its conformational change and ligand binding cleft. Thus, in the light of data presented in Table 1 and the additional disclosure herein, the resting I-domain co-ordinates [26] becomes a useful reference point for rational drug design. This allows certain surfaces, defined by the residues presented in Table 1, but whose resting co-ordinates are contained in 1aox, to be identified unambiguously as contributing to the latent ligand binding cleft. Hence an inhibitor may be designed to bind to the resting I-domain and so prevent it from binding ligand.

For other I-domains, regions corresponding to those identified for α2 I-domain as targets for antibody molecules are identified in accordance with the present invention as:

αM: residues 301-304 (N-terminal end of Helix α7),
residues 272-284 (N-terminal end of Helix α6);

αL: residues 290-295 (N-terminal end of Helix α7),
residues 258-272 (N-terminal end of Helix α6);

α1: residues 318-324 (N-terminal end of Helix α7),
residues 292-298 (N-terminal end of Helix α6).

Thus, an antibody molecule or other binding molecule may be obtained, e.g. by making a peptide comprising or consisting of the above residues of any of the above regions and bringing the peptide into contact with a mixture containing potential binding molecules, determining binding to the peptide and selecting a binding molecule that binds. A binding molecule such as an antibody molecule may be tested for ability to bind and inhibit an I-domain, and may be employed as an inhibitor of a polypeptide comprising an I-domain for one or more

purposes as disclosed herein.

Specific residues can also be identified, such as T221 in α2 I-domain, linked to metal ion in the resting I-domain indirectly via a water molecule. Suitable inhibitors may be designed to bind T221 and prevent the metal ion from moving closer to become co-ordinated directly. Such inhibitors may be used to prevent subsequent ligand binding.

Comparison of the crystal structure of the integrin a2 I-domain in complex with the triple-helical collagen-like peptide with that of the free, uncomplexed, I-domain [26] allows regions of the I-domain to be identified which may be exposed in the free state, but which become hidden in the complexed state. An example will be those areas of the surface of the I-domain which are obscured by the binding of the triple-helical peptide. These specific residues are identified in Table 2. Other such sites are remote from the binding cleft, and are revealed by conformational changes which occur during the transition from the free to the complexed state. Such sites may also represent therapeutic targets: agents such as inhibitors or antibodies which bind to these critical exposed regions of the complexed integrin may block the transition to the resting conformation, so maintaining the integrin in its active conformation.

The present invention allows such residues to be identified, and the co-ordinates of the I-domain surface in these regions to be used for rational drug design, as described above.

Alternatively, as noted, knowledge of these critical regions of the I-domain allows peptide sequences to be used to raise antibodies or other binding molecules by appropriate

methodology, for example against short peptide sequences derived from the I-domain or by DNA vaccination of nucleotide sequences corresponding to these regions of the I-domain. The utility of such inhibitors may be tested as described above, in suitable adhesion or other assays.

Reference to an Aantibody molecule@ describes an immunoglobulin whether natural or partly or wholly synthetically produced. The term also covers any polypeptide or protein having a binding domain which is, or is substantially homologous to, an antibody binding domain. Thus, antibody molecules for use in the present invention include fragments which comprise an antigen binding domain such as Fab, scFv, Fv, dAb, Fd and diabodies, all of which are well known in the art.

Comparison of the two forms of the integrin I-domain allows sites to be identified upon its surface which are hidden in the free integrin, and which are exposed only after complex with suitable ligand, for example the triple-helical peptide described above, Ac-$(GPO)_2$GFOGER$(GPO)_3$-NH_2. Such sites, when targeted by inhibitors may have two possible effects: if sufficiently close or within the binding cleft, they may inhibit ligand binding, but if sufficiently remote so as not to impede ligand binding, they may stabilise the integrin in its active conformation and so enhance ligand binding. Such activity may be identified by binding assays as described herein, and each class of agent, whether inhibitory or activatory towards integrin function, may have its own therapeutic use or other application.

Regions of interest within the α2 I-domain binding cleft are identified in Table 2, which also lists residues of the I-

domain (E318 and D292) which are exposed upon ligand binding and are not obscured by the triple-helical peptide.

A collagen peptide employed in testing for ability of a potential inhibitor to inhibit binding of the I-domain to the peptide may be a triple-helical peptide, of sequence GFOGER known to bind the α2 I-domain [18], or other sequence which binds to the I-domain, flanked by suitable repeats of GPO or GPP triplets to ensure triple-helical structure. Alternatively, physiological substrates such as collagens, for example type I or type III or type IV or type VI or other collagens, readily coat and adhere to the surface of tissue culture dishes or 96-well plates, and are known to bind to α2β1. Alternatively, other substrates such as the extracellular protein laminin, also known to bind the I-domain of α2β1, may be used for the same purpose. Specificity of interaction in this and other assays may be verified by using antibodies against either the immobilised substrate or the receptor on the surface of cells under test.

In any aspect of the present invention a potential inhibitor that tests positive when brought into contact with the I-domain, that is fulfils one or more of the specified criteria, is considered an actual inhibitor.

Thus further aspects of the present invention provide methods of identifying and/or obtaining inhibitors of a polypeptide which contains an I-domain, especially an Integrin, which may be selected from the group consisting of α1, α2, α10, α11, αD, αE, αL, αM and αX, especially α2 or α1, most preferably α2.

Another aspect of the present invention provides a crystal of

α2 I-domain complex having a space group $P2_12_12_1$, and unit cell dimensions of a = 42.0 Å, b = 48.4 Å, and c = 114.5 Å. Or more generally a = 42.0±0.2 Å, b = 48.4±0.2 Å, and c = 114.5±0.2 Å.

Alternatively or additionally, the present invention provides a crystal of α2 I-domain complex having the three dimensional atomic coordinates of Table 1.

Further aspects of the present invention provide (i) a computer system, intended to generate structures and/or perform rational drug design for I-domain-containing polypeptides or I-domain-containing polypeptide complexes, the system containing atomic coordinate data according to Table 1 or Table 2, and (ii) computer readable media for use in the computer system, having atomic coordinate data according to Table 1 or Table 2 recorded thereon.

By a "computer system" we mean the hardware means, software means and data storage means used to analyse atomic coordinate data. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means and data storage means. Desirably a monitor is provided to visualise structure data. The data storage means may be RAM or means for accessing computer readable media of the invention. Examples of such systems are microcomputer workstations available from Silicon Graphics Incorporated and Sun Microsystems running Unix based, Windows NT or IBM OS/2 operating systems.

By "computer readable media" we mean any media which can be read and accessed directly by a computer e.g. so that the

media is suitable for use in the above-mentioned computer system. Such media include, but are not limited to: magnetic storage media such as floppy discs, hard disc storage medium and magnetic tape; optical storage media such as optical discs or CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media.

By providing such a system or such computer readable media, the atomic coordinate data can be routinely accessed to model I-domain-containing polypeptides and complexes thereof, e.g. using the molecular graphics programs discussed above.

Another aspect of the present invention provides an inhibitor of an I-domain identified or obtained by any method disclosed herein.

An inhibitor may be formulated into a composition comprising at least one additional component.

Following identification of an inhibitor it may be manufactured and/or used in preparation, i.e. manufacture or formulation, of a composition such as a medicament, pharmaceutical composition or drug. These may be administered to individuals.

Thus, the present invention extends in various aspects not only to an inhibitor as provided by the invention, but also a pharmaceutical composition, medicament, drug or other composition comprising such an inhibitor, a method comprising administration of such a composition to a patient, e.g. for treatment (which may include preventative treatment) of a disorder or disease, use of such an inhibitor in manufacture

of a composition for administration, e.g. for treatment of a disorder or disease, and a method of making a pharmaceutical composition comprising admixing such an inhibitor with a pharmaceutically acceptable excipient, vehicle or carrier, and optionally other ingredients.

Disorders and diseases which may be treated in accordance with aspects of the present invention include the thrombotic disorders, myocardial infarction and stroke, acute thrombosis associated with angioplasty and with coronary bypass grafting, and with liver fibrosis or thrombotic complication of liver necrosis each of which is prone to occur after hepatitis infection. Inhibition of platelet $\alpha 2\beta 1$ may be used to treat longer-term occlusion of arteries, restenosis which commonly occurs after angioplasty as well as atherogenesis as a consequence of arterial vascular smooth muscle cell migration from the medial to the intimal space. Collagen receptor antagonism may be used to provide a novel means of anti-platelet therapy, and to be of benefit in clinical situations where conventional anti-platelet therapy is also effective.

The integrin $\alpha 2\beta 1$, and the closely-related $\alpha 1\beta 1$, for which GFOGER-containing triple-helical peptide is also a ligand, are widely expressed in mammalian cells. These integrins each provide a means of adhesion and migration of cells over the underlying collagen-containing extracellular matrix, and as such, may be essential for the metastasis of tumour cells. Inhibitors of $\alpha 2$ and $\alpha 1$ I-domain function may be used to inhibit metastasis.

As discussed herein, the present invention will also apply to other I-domains, such as those of αL and αM, inhibition of which will lead to down-regulation of those aspects of

leukocyte function which depend upon cell adhesion. Therapeutically, such aspects of the present invention may be used to prevent excessive leukocyte (both monocyte and neutrophil) infiltration across vascular endothelia which may result in excessive tissue necrosis in sepsis; inhibition may be valuable in controlling inflammation.

An inhibitor of a polypeptide (e.g. Integrin $\alpha 2\beta 1$) may be used in treatment of a disease or disorder in which the polypeptide has a role, and may be administered to any individual, human or non-human, in need thereof.

When an inhibitor according to the present invention is to be given to an individual, administration is preferably in a Aprophylactically effective amount@ or a "therapeutically effective amount" as the case may be, although prophylaxis may be considered therapy), this being sufficient to show benefit to the individual. The actual amount administered, and rate and time-course of administration, will depend on the nature and severity of what is being treated. Prescription of treatment, e.g. decisions on dosage etc., is within the responsibility of general practitioners and other medical doctors.

A composition may be administered alone or in combination with other treatments, either simultaneously or sequentially dependent upon the condition to be treated.

Pharmaceutical compositions according to the present invention, and for use in accordance with the present invention, may include, in addition to active ingredient, a pharmaceutically acceptable excipient, carrier, buffer, stabiliser or other materials well known to those skilled in

the art. Such materials should be non-toxic and should not interfere with the efficacy of the active ingredient. The precise nature of the carrier or other material will depend on the route of administration, which may be oral, or by injection, e.g. cutaneous, subcutaneous or intravenous.

Pharmaceutical compositions for oral administration may be in tablet, capsule, powder or liquid form. A tablet may include a solid carrier such as gelatin or an adjuvant. Liquid pharmaceutical compositions generally include a liquid carrier such as water, petroleum, animal or vegetable oils, mineral oil or synthetic oil. Physiological saline solution, dextrose or other saccharide solution or glycols such as ethylene glycol, propylene glycol or polyethylene glycol may be included.

For intravenous, cutaneous or subcutaneous injection, or injection at the site of affliction, the active ingredient will be in the form of a parenterally acceptable aqueous solution which is pyrogen-free and has suitable pH, isotonicity and stability. Those of relevant skill in the art are well able to prepare suitable solutions using, for example, isotonic vehicles such as Sodium Chloride Injection, Ringer's Injection, Lactated Ringer's Injection. Preservatives, stabilisers, buffers, antioxidants and/or other additives may be included, as required.

Examples of techniques and protocols mentioned above can be found in Remington=s Pharmaceutical Sciences, 16th edition, Osol, A. (ed), 1980.

The basis for considering that the principles established here for α2 I-domain will be applicable to other receptors is two-

fold. Firstly, the surface of the several I-domains under consideration is very similar. On these grounds alone it is anticipated that antagonists of α2 I-domain will also inhibit other I-domains. Secondly, experiment has demonstrated that this principle does extends to the α1 I-domain, since the triple-helical GFOGER-containing peptide supports adhesion of Ruggli cells mediated by α1β1, and inhibits adhesion of these same cells to collagen and of the purified receptor to collagen [18]. Other collagen-binding I-domains α10, α11 are expected to follow suit.

Receptor antagonists of α2 I-domain provide for identification of antagonists of other I-domains, and the surface of the α2 I-domain embodied in Table 2 will provide valuable assistance in the model building exercise needed for rational drug design targeting these ubiquitous cellular adhesion receptors.

Further aspects and embodiments of the present invention will be apparent to those skilled in the art. The invention will now be illustrated further with reference to experimental support and use of aspects and embodiments of the invention.

Brief Description of Drawings

Figure 1 shows the melting curve for peptide Ac-$[GPO]_2$GFOGER$[GPO]_3$-NH_2. The Figure shows the variation in optical rotation with temperature of a solution of the peptide, indicating the transition from triple helical to random coil conformation as temperature increases.

Figure 2 shows the structure of the α2 I-domain in complex with the triple helical synthetic peptide. Beta strands

within the I-domain are shown as broad arrows, and alpha-helices as coiled ribbons. The backbones only of other loops of the I-domain and of the strands of the triple helical peptide are shown.

Figure 3 shows that interaction of α2 I-domain and peptide is confined to two strands of triple-helix. The Figure shows the surface of the α2 I-domain in complex with the triple helical synthetic peptide. The footprint of the triple helical peptide on the I-domain surface is shaded, and both sidechains and peptide carbonyls which interact with the I-domain are indicated by arrows.

Figure 4 shows that carbonyl groups on Middle and Trailing strands of the triple-helix interact with I-domain Y185 and H258. Interactions are shown as dashed lines.

Figure 5 illustrates principal conformational changes in I-domain upon binding of peptide. The Figure shows the three-dimensional structure of the α2 I-domain in its resting, un-ligated form (grey) superimposed on the structure after ligation (dark) with triple-helical Ac-$[GPO]_2GFOGER[GPO]_3$-NH_2. The peptide is not shown. I-domain α-helices (with their numbers above them) are shown as coiled ribbons, and β-strands as broad arrows. Conformational changes are indicated by outlined arrows.

Figure 6 shows details of the α2 I-domain MIDAS after ligation with triple-helical Ac-$[GPO]_2GFOGER[GPO]_3$-NH_2. The peptide glutamate (E) is shown, along with the residues of the I-domain which also co-ordinate the metal ion in the ligated (peptide-bound) state of the I-domain. Amino acids of the I-

domain involved in metal ion co-ordination are indicated by letters (single amino-acid nomenclature) and numbers defining their position within the I-domain sequence. Interactions are indicated by dashed lines.

Experimental Support and Use of Aspects and Embodiments of the Invention

Design, Production and Analysis of a Triple Helical Peptide that Binds and Crystallises with Integrin I Domain

The peptide Ac-$(GPO)_2$GFOGER$(GPO)_3$-NH_2 was synthesized (see below for materials and methods) and shown to adopt triple helical conformation, as demonstrated by the melting curve (Figure 1). This indicated that at cold-room temperature, i.e. below 10°C, more than 90 % of the peptide was in triple helical conformation, determined by optical polarimetry. Other methods such as circular dichroism may be used to provide further confirmation of the triple-helical state of the peptide.

Crystallisation of the Peptide of Example 1 and the I-domain of Integrin α2 and Determination of Atom Co-ordinates

Materials and methods are described below.

The co-ordinates of the atoms comprising:
(i) the triple-helical structure of peptide
Ac-$(GPO)_2$GFOGER$(GPO)_3$-NH_2 ,
(ii) the I-domain of the integrin α2 subunit, comprising residues 143 to 326 of the integrin sequence,
(iii) water molecules forming part of the crystal complex, and
(iv) a metal ion bridging the I-domain and collagen.

are shown in Table 1.

The deduced 3-dimensional structure of the complex is shown in Figures 2 - 6.

The collagen-like peptide adopts its characteristic triple-helical structure with a 1-residue displacement between strands, these being in parallel rather than anti-parallel alignment. This allows us to define the strands as leading, middle and trailing, with the trailing strand being displaced towards the N-terminus of the triple-helix, relative to the middle strand, and the leading strand displaced towards the C-terminus of the trimeric structure. This is illustrated in Figure 2.

In turn, this allows the strands to be seen as non-equivalent; the environment of any specific amino acid is defined by its relationship with different amino acids in each adjacent strand, and so the structure is lacking in radial symmetry. The significance of this is that, if the amino acids interacting with the I-domain were confined to a single strand, any of the three strands could serve this function, and crystallisation would be unlikely, given that there would be three, non-equivalent peptide:I-domain complexes as a consequence of the stagger between the different strands.

If two strands engage the I-domain, then two of the three possible orientations of the helix will suffice (after axial rotation by 120° and translation of the helix by one residue) but the third orientation will be non-identical and unfavourable.

If three strands engage the I-domain, then a unique complex

will result.

Surprisingly, given that crystal formation of the α2 I-domain:peptide complex is observed, the second possibility proves to be the case. Complex formation could in principle occur in either of two conformations, therefore. The successful crystallisation shows that only one of the two possible orientations occurs within the complex is allowed and suggests that interaction between the ends of adjacent triple-helices within the crystal lattice favours one of the two possible complexes.

This helix:helix interaction is permitted by the unique overlap between the C-termini of triple-helical peptides in adjacent unit cells, which are related by a two-fold axis. This may be the cause of the bend seen in the complexed helix, although it is also possible that interactions of the triple-helix with the I-domain support this perturbation of the triple-helix linear structure.

Interaction with the I-domain is restricted to the middle and trailing strands. Multiple sites of interaction are shown in Figure 3. These include interactions of carbonyl groups from the peptide bonds of the triple helix with specific residues within the I-domain (some of which are shown in detail in Figure 4), as well as the key interactions of the middle strand E (which co-ordinates the metal ion) and R residue (which forms a salt-bridge with I-domain D219)and trailing strand F residue. An inhibitor of receptor interaction with collagen and/or function may inhibit one or more of these interactions, and this may be by making the interactions.

The changes in the α2 I-domain upon ligation by the GFOGER-

containing peptide may be summarised thus:

Upon complex formation between the I-domain and the collagen-like peptide, the C-Helix unwinds while the connecting loop coils up to form an extra turn of Helix α6.

Helix α7 undergoes a remarkable displacement upon ligand binding. This helix translates axially towards the base of the I-domain (the C-terminal end of the beta-sheet) by almost its own length, a distance of about 1 nm.

The residues responsible for co-ordinating the cation in the MIDAS are re-arranged, allowing the glutamate residue of the collagen sequence GFOGER to approach the apex of, and so complete, the octahedral co-ordination shell of the divalent cation.

An overview of these changes is shown in Figure 5.

The detail of these changes is provided as follows: Comparison between the collagen-bound and unligated α2 I-domain shows that the central beta-sheet does not change its conformation upon ligation (RMSD = 0.03 nM), providing a convenient reference frame for structural comparison.

The structural changes on binding ligand may be described as follows. The metal ion moves 0.26 nm towards MIDAS Loop 2 in order to make a direct bond with T221. MIDAS Loop 1 follows the movement of the metal in order to maintain its direct bonds via S153 and S155. MIDAS Loop 3 undergoes a radical rearrangement: the sidechain of D254 moves laterally so that its direct bond to the metal is lost; the G255 peptide bond flips by 180E so that its Cα moves ~0.4 nm away from the metal

ion; and E256 forms a new water-mediated bond to the metal. The outcome of these events is shown in Figure 6. The movement of Loop 1 towards Loop 3 brings the side chains of Y157 and H258 0.3 nm closer together such that they both fit into grooves of the triple helix.

The shift of Loop 1 and the rearrangement of Loop 3 trigger a reorganization of the C-helix and Helix α7. Loop 1 is packed against α7 in the unliganded structure, and the large concerted movement of Loop 1 and Helix a1 appears to Asqueeze out@ the α7 helix, and it drops downwards by 1 nm. This movement breaks a partly buried salt bridge between E318 from α7 and R288 from the C-helix. The flip of Loop 3, which is packed closely against Helix α6, forces a rearrangement of the sidechain of the buried L296 that would create a close contact with L286 from the C-helix. In response to the steric pressure between these leucines, and the loss of the stabilizing E318-R288 salt-bridge, the C-helix unwinds while the connecting loop coils up to form an extra turn at the N-terminus of helix α6. The uncoiling of the C-helix produces a dramatic 180E rotation and shift of Y285, such that its hydroxyl oxygen moves by 1.7 nm from its location above the MIDAS motif to form a hydrogen bond with S316 at the top of the repositioned α7. By contrast, L286 moves 0.4 nm towards the collagen, where it makes van der Waals contacts with the trailing strand phenylalanine, and R288 moves 0.6 nm closer to the MIDAS motif, where it forms a water-mediated salt-bridge to D254.

Inhibition of any one or more of these structural changes may be used to inhibit receptor interaction with collagen and/or function. An inhibitor or receptor function may inhibit

totally or partially one or more of the conformational changes.

Discussion

Several notable features of the structure are revealed, which shed light upon the function of the I-domain as a dynamic piece of cellular machinery, capable of regulating cell function, and whose own function may be regulated by the cell. These conclusions arise from the comparison of the ligated and unligated structures of the α2 I-domain, detailed above.

Firstly, it appears that the role of the C-helix is to regulate ligand binding, since it controls access to the MIDAS. Secondly, the translation of Helix 7 upon ligand binding could serve either of two functions, to regulate the position of the C-helix from within the cell, i.e. to increase the affinity of the integrin, or to transmit signals from the ligated MIDAS to the body of the integrin and thence to the cell. Plausibly, the same molecular movement could serve both purposes.

This level of understanding supports several approaches to rational drug design, assuming that the therapeutic intent is to inhibit integrin function.

Firstly, small molecule analogues of collagen may be designed, of similar shape and charge distribution to the key residues of the sequence GFOGER, which bind to the complementary structure, the binding cleft of the α2 I-domain. Solution of the complex structure provided here enables establishment of the critical determinants of ligand binding, location of key atomic interactions and assignment of binding energies. This

information provides for in silico construction of integrin α2β1 antagonists, preferably focussing upon the integrin MIDAS.

Secondly, molecules that inhibit the conformational changes described may be designed. For example, small molecule ligands may be designed for regions adjacent to the C-helix to stabilise it in the closed conformation so preventing ligand binding, as discussed already herein. This approach offers an alternative to direct antagonism of the MIDAS.

Similarly, the regions of the I-domain at the C-terminus of Helix α7 (close to the interface between the I-domain and the rest of the integrin α2 subunit) may be targeted. This enables design of small molecules which prevent translation of the helix from occurring, with the consequence of locking the integrin in its inactive conformation, preventing both collagen binding and inwards signal transduction from taking place.

Furthermore, the different integrins characterised to date parallel one another in both structure and function. Hence, the other I-domain-containing integrins, known at present to include α1, α2, α10, α11, αD, αE, αL, αM and αX, may be targetted in accordance with the present invention. For instance an inhibitor of α2 or α1 identified using the present invention may be tested for ability to inhibit one or more other integrins containing an I-domain. Additionally, the data presented here allow predictions to be made concerning the active (ligated) form of the integrin based upon the conformation of the resting integrin, or from primary sequence using the co-ordinates of known structures such as α2 I-domain

or αL I-domain as a model. Thus a region of an I-domain considered by analogy with the ligated α2 I-domain crystal structure information presented herein to be involved in ligand binding and/or involved in a conformational change on ligand binding, may be targeted, for instance by means of an antibody or other specific binding molecule.

These concepts may be extended to other, non-integrin proteins, such as von Willebrand factor, which contain I-domains and which might undergo activation in an analogous fashion.

The knowledge of the structural changes occurring in the integrin upon ligation presented here provides such proteins as targets for rational drug design.

Materials and Methods

Crystallization and data collection

Recombinant α2-I domain and a synthetic collagen-like peptide, Ac-$(GPO)_2$GFOGER$(GPO)_3$-NH_2, were produced [18, 26]. See also WO99/50281. Crystallization experiments were performed at 4EC using the sitting drop vapor diffusion method. Initial conditions were established using a 2 ml sample of protein in buffer 0.1 M Tris pH 7.5, 0.15M NaCl, 2 mM $MgCl_2$ (or $MnCl_2$) and peptide in 10 mM acetate pH 5.0 mixed in a ratio of 1:4 added to 2 ml of well solution consisting of 25 mM sodium cacodylate pH 6.5, 20% glycerol and 20-30% PEG 5K MME. Small bunched crystals appeared after 2-4 days and had flattened rod-like morphology with dimensions 0.025 x 0.025 x 0.1 mm^3. The crystals adopt space group $P2_12_12_1$ with cell dimensions a = 4.2 nm, b = 4.84 nm, c = 11.45 nm. Crystal growth was dependent on

the presence and concentration of divalent cation but was unaffected by the cation species. Similar crystals grew in the presence of Mg^{2+}, Mn^{2+}, Co^{2+}, Cd^{2+}, Ni^{2+} and Zn^{2+} ions. Larger single crystals were rare and improved only marginally by making small changes in the cation concentration and the protein:peptide ratio. Data were collected at the Daresbury Synchrotron Radiation Source using a single crystal flash frozen in a cryo-stream of nitrogen at a temperature of 100 K. Data set Native I was collected from station 9.6 using the Quantum4 CCD detector to 0.25 nm resolution. This crystal was grown in 1 mM $ZnCl_2$ using a protein to triple helical peptide ratio of 1:2.5. A high resolution data set to 0.21 nm resolution (Native II) was subsequently collected on SRS station 7.2 using a MAR345 scanner. This crystal was grown in 1 mM $CoCl_2$ using a protein to peptide ratio of 1:1.6. Data were reduced with DENZO and scaled with SCALEPACK [29]. The overall I/sI for Native II is 12.0 (2.9 in 2.17-2.1 A shell) with an R_{merge} of 8.9% (34.4% in outer shell), an average redundancy of 2.9 and completeness of 98.2% in the range 20-2.1 A (14483 reflections).

Structure determination and refinement

Molecular replacement was performed on the Native I data set with AMORE [30] using the crystal structure of the uncomplexed α2-I domain as the search model. A clear solution was found in the cross rotation function and subsequent translation function. The initial R_{WORK} was 52.0% with an R_{FREE} of 54.2%. A $2F_o$-F_c electron density map calculated at 0.25 nm was of high quality with changes in the MIDAS motif readily apparent. Little density for the collagen peptide could be observed in the $2F_o$-F_c or F_o-F_c map at this stage. Several rounds of model building and refinement of the I domain using XTALVIEW [31]

resulted in greatly improved density for several regions of the domain which had undergone structural change. Following rebuilding of the I domain some density for the collagen peptide was apparent in the $2F_o$-F_c and F_o-F_c electron density maps. Solvent flattening using a molecular mask constructed to encompass the predicted peptide region provided unbiased improvement of the peptide electron density, and 24 alanine residues were inserted. At this stage the identification of hydroxyproline hydroxyl groups in the C-terminal GPO triplets allowed the correct assignment of the collagen chain direction. Identification of GFOGER sidechain density and the C-terminal ends of each chain allowed correct positioning of the leading, middle and trailing strands. Several rounds of model building and refinement allowed complete identification of the collagen peptides. At this stage data to 0.21 nm resolution became available from the native II data set showing an initial R_{WORK} of 38.6% and an R_{FREE} of 47.1% against the refined model. Further cycles of model building and refinement, including the insertion of 398 water molecules, gave a final R_{WORK} of 0.203 and R_{FREE} of 0.276 (5% of the reflections). The RMS deviations from ideal bond length and angles are 0.0006 nm and 1.41E. Good density is observed for I domain residues 142 to 326 and for all collagen residues, although the N-terminal GPO triplet of each strand is more mobile than the others. The coordinates and structure factors have been deposited with the PDB (code assigned; 1dzi).

References

1. WO99/50281
2. Barnes (1988) in *Collagen, Vol 1: Biochemistry,* M.E. Nimni, Ed. CRC press: Boca Raton, Fl. p. 275-290.
3. Knight *et al.* (1999) Cardiovasc. Res. **41**:450-457.
4. Werkmeister & Ramshaw (1991) Biochem. J. **274**:895-898.
5. Bella *et al.* (1994) Science **266**:75-81.
6. Yang *et al.* (1997) J. Biol. Chem. **272**:28837-28840.
7. Morton *et al.* (1995) Biochem. J. **306**:337-344.
8. Kehrel *et al.* (1998) Blood **91**:491-499.
9. Gibbins *et al.* (1997) FEBS Lett. **413**:255-259.
10. Gibbins *et al.* (1996) J. Biol. Chem. **271**:18095-18099.
11. Erb *et al.* (1997) Biochemistry **36**:7395-7402.
12. Sixma *et al.* (1997) Thromb. Haemost. **78**:434-438.
13. Moroi & Jung (1997) Thromb. Haemost. **78**:439-444.
14. Barnes *et al.* (1998) Curr. Opin. Haematol. **5**:314-320.
15. Fields *et al.* (1993) J. Biol. Chem. **268**:14153-14160.
16. Morton *et al.* (1997) J. Biol. Chem. **272**:11044-11048.
17. Knight *et al.* (1998) J. Biol. Chem. **273**:33287-33294.
18. Knight *et al.* (2000) J. Biol. Chem. **275**:35-40.
19. Hynes (1992) Cell **69**:11-25.
20. Humphries (1990) J. of Cell Science **97**:585-592.
21. Kuhn K & Eble J (1994) Trends in Cell Biol. **4**:256-261.
22. Casasnovas *et al.* (1997) Nature **387**:312-315.
23. Springer (1997) Proc. Natl. Acad. Sci. (USA) **94**:65-72.
24. Fujimura & Phillips (1983) J. Biol. Chem. **258**:10247-10252.
25. Tuckwell *et al.* (1995) J. Cell Sci. **108**:1629-1637.
26. Emsley *et al.* (1997) J. Biol. Chem. **272**:28512-28517.
27. Dickeson *et al.* (1997) J. Biol. Chem. **272**:7661-7668.
28. Ducruix & Giege (1992) in *Crystallisation of nucleic acids and proteins: A practical approach.* IRL press: Oxford.

29. Otwinowski (1993) in *Data collection and processing*, L. Sawyer, N. Isaacs, andS. Bailey, Ed. SDERC: Daresbury, UK. p. 59-62.

30. Navaza (1994) Acta Cryst. **A50**:157-163.

31. McRee (1999) J. Struct. Biol. **125**:156-165.

All documents cited anywhere in this text are incorporated by reference.

TABLE 1 - Co-ordinates of the crystal formed from the α2 I-domain and triple-helical peptide Ac-$(GPO)_2$GFOGER$(GPO)_3$-NH_2 in complex.

The sequence of each molecular component of the crystal complex is provided:

Fifteen consecutive lines define the amino acid sequence beginning with the N-terminal Alanine (ALA) of the recombinant I-domain, which contains 185 amino acid residues and is defined as A.

Two consecutive lines define the sequence of the 21 amino acids and C-terminal amide of the first chain of the triple helical peptide, defined as B.

Four further consecutive lines define identically the sequence of the second and third chains of the triple-helical peptide, defined as C and D.

Thirty-one lines show the water molecules (HOH) which are comprised within the structure of the complex as water of crystallisation, defined collectively as E.

One line defines the cobalt ion (CO) as F.

One line (CRYST1) defines the dimensions of the crystal cell, and its spacegroup.

Atoms comprising the crystal complex are listed sequentially, identified in Columns 1 and 2; Column 3 defines each specific atom within an amino acid residue; Column 4 defines the identity and position of the amino acid within the sequence,

or of other chemical species such as water (HOH), and the chain (defined above as A, B, C, D, E or F) containing the specific atom; Columns 5, 6 and 7 provide the X, Y and Z co-ordinates respectively of the specific atom; Column 8 provides the occupancy, that is presence or absence for the purposes of analysis; Column 9 provides a parameter of thermal mobility known as the B-factor; Column 10 provides an alternative means of identifying the chain in which the atom resides, useful for certain computer software packages (A defines atoms as being within Chain A, the I-domain: CA, CB and CD identify atoms as residing within the triple-helical peptide chains, Collagen A, Collagen B or Collagen C: W defines an atom as belonging to water, and M as being the metal ion).

```
SEQRES   1 A  185  ALA LEU ILE ASP VAL VAL VAL VAL CYS ASP GLU SER ASN
SEQRES   2 A  185  SER ILE TYR CPR TRP ASP ALA VAL LYS ASN PHE LEU GLU
SEQRES   3 A  185  LYS PHE VAL GLN GLY LEU ASP ILE GLY PRO THR LYS THR
SEQRES   4 A  185  GLN VAL GLY LEU ILE GLN TYR ALA ASN ASN PRO ARG VAL
SEQRES   5 A  185  VAL PHE ASN LEU ASN THR TYR LYS THR LYS GLU GLU MET
SEQRES   6 A  185  ILE VAL ALA THR SER GLN THR SER GLN TYR GLY GLY ASP
SEQRES   7 A  185  LEU THR ASN THR PHE GLY ALA ILE GLN TYR ALA ARG LYS
SEQRES   8 A  185  TYR ALA TYR SER ALA ALA SER GLY GLY ARG ARG SER ALA
SEQRES   9 A  185  THR LYS VAL MET VAL VAL VAL THR ASP GLY GLU SER HIS
SEQRES  10 A  185  ASP GLY SER MET LEU LYS ALA VAL ILE ASP GLN CYS ASN
SEQRES  11 A  185  HIS ASP ASN ILE LEU ARG PHE GLY ILE ALA VAL LEU GLY
SEQRES  12 A  185  TYR LEU ASN ARG ASN ALA LEU ASP THR LYS ASN LEU ILE
SEQRES  13 A  185  LYS GLU ILE LYS ALA ILE ALA SER ILE PRO THR GLU ARG
SEQRES  14 A  185  TYR PHE PHE ASN VAL SER ASP GLU ALA ALA LEU LEU GLU
SEQRES  15 A  185  LYS ALA GLY
SEQRES   1 B   22  GLY PRO HYP GLY PRO HYP GLY PHE HYP GLY GLU ARG GLY
SEQRES   2 B   22  PRO HYP GLY PRO HYP GLY PRO HYP NHH
SEQRES   1 C   22  GLY PRO HYP GLY PRO HYP GLY PHE HYP GLY GLU ARG GLY
SEQRES   2 C   22  PRO HYP GLY PRO HYP GLY PRO HYP NHH
SEQRES   1 D   22  GLY PRO HYP GLY PRO HYP GLY PHE HYP GLY GLU ARG GLY
SEQRES   2 D   22  PRO HYP GLY PRO HYP GLY PRO HYP NHH
SEQRES   1 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   2 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   3 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   4 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   5 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   6 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   7 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   8 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   9 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  10 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
```

```
SEQRES  11 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  12 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  13 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  14 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  15 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  16 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  17 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  18 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  19 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  20 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  21 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  22 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  23 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  24 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  25 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  26 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  27 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  28 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  29 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  30 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES  31 E  400  HOH HOH HOH HOH HOH HOH HOH HOH HOH HOH
SEQRES   1 F    1  CO

CRYST1   41.994   48.377  114.545  90.00  90.00  90.00 P 21 21 21    24

ATOM      1  CB  ALA A 142      11.648 -13.520  47.836  1.00 34.96      A
ATOM      2  C   ALA A 142       9.671 -12.738  49.142  1.00 34.94      A
ATOM      3  O   ALA A 142       8.835 -13.081  49.983  1.00 35.57      A
ATOM      4  N   ALA A 142       9.402 -13.644  46.820  1.00 35.53      A
ATOM      5  CA  ALA A 142      10.165 -13.735  48.096  1.00 34.99      A
ATOM      6  N   LEU A 143      10.173 -11.504  49.092  1.00 33.30      A
ATOM      7  CA  LEU A 143       9.763 -10.523  50.085  1.00 30.95      A
ATOM      8  CB  LEU A 143      10.863 -10.384  51.155  1.00 30.60      A
ATOM      9  CG  LEU A 143      12.286  -9.955  50.765  1.00 31.70      A
ATOM     10  CD1 LEU A 143      12.375  -8.444  50.664  1.00 32.35      A
ATOM     11  CD2 LEU A 143      13.275 -10.423  51.811  1.00 30.98      A
ATOM     12  C   LEU A 143       9.304  -9.133  49.630  1.00 29.03      A
ATOM     13  O   LEU A 143       8.144  -8.776  49.845  1.00 28.59      A
ATOM     14  N   ILE A 144      10.174  -8.354  48.992  1.00 26.76      A
ATOM     15  CA  ILE A 144       9.788  -6.988  48.623  1.00 24.45      A
ATOM     16  CB  ILE A 144      10.354  -5.982  49.660  1.00 24.71      A
ATOM     17  CG2 ILE A 144       9.884  -4.583  49.339  1.00 24.79      A
ATOM     18  CG1 ILE A 144       9.898  -6.365  51.072  1.00 25.36      A
ATOM     19  CD1 ILE A 144      10.517  -5.520  52.173  1.00 25.41      A
ATOM     20  C   ILE A 144      10.151  -6.446  47.238  1.00 22.83      A
ATOM     21  O   ILE A 144      11.317  -6.426  46.842  1.00 22.87      A
ATOM     22  N   ASP A 145       9.135  -5.980  46.520  1.00 19.93      A
ATOM     23  CA  ASP A 145       9.330  -5.386  45.210  1.00 18.20      A
ATOM     24  CB  ASP A 145       8.371  -6.002  44.181  1.00 17.90      A
ATOM     25  CG  ASP A 145       8.865  -7.340  43.639  1.00 18.99      A
ATOM     26  OD1 ASP A 145      10.071  -7.645  43.799  1.00 21.43      A
ATOM     27  OD2 ASP A 145       8.056  -8.077  43.034  1.00 16.50      A
ATOM     28  C   ASP A 145       9.056  -3.886  45.363  1.00 17.28      A
ATOM     29  O   ASP A 145       7.903  -3.463  45.478  1.00 16.93      A
ATOM     30  N   VAL A 146      10.120  -3.087  45.383  1.00 16.46      A
ATOM     31  CA  VAL A 146       9.981  -1.644  45.542  1.00 15.31      A
```

ATOM	32	CB	VAL	A	146	10.946	-1.092	46.615	1.00	16.68	A
ATOM	33	CG1	VAL	A	146	10.681	0.395	46.826	1.00	17.60	A
ATOM	34	CG2	VAL	A	146	10.780	-1.846	47.916	1.00	17.29	A
ATOM	35	C	VAL	A	146	10.231	-0.848	44.268	1.00	14.93	A
ATOM	36	O	VAL	A	146	11.275	-0.984	43.630	1.00	14.75	A
ATOM	37	N	VAL	A	147	9.270	-0.002	43.916	1.00	13.85	A
ATOM	38	CA	VAL	A	147	9.385	0.846	42.741	1.00	13.06	A
ATOM	39	CB	VAL	A	147	8.215	0.624	41.751	1.00	14.12	A
ATOM	40	CG1	VAL	A	147	8.284	1.650	40.628	1.00	12.57	A
ATOM	41	CG2	VAL	A	147	8.270	-0.797	41.184	1.00	13.32	A
ATOM	42	C	VAL	A	147	9.384	2.309	43.165	1.00	12.08	A
ATOM	43	O	VAL	A	147	8.431	2.784	43.791	1.00	12.23	A
ATOM	44	N	VAL	A	148	10.468	3.004	42.831	1.00	11.18	A
ATOM	45	CA	VAL	A	148	10.625	4.424	43.130	1.00	9.94	A
ATOM	46	CB	VAL	A	148	12.106	4.779	43.401	1.00	10.37	A
ATOM	47	CG1	VAL	A	148	12.258	6.282	43.621	1.00	10.02	A
ATOM	48	CG2	VAL	A	148	12.608	4.016	44.615	1.00	11.21	A
ATOM	49	C	VAL	A	148	10.144	5.254	41.942	1.00	10.76	A
ATOM	50	O	VAL	A	148	10.622	5.078	40.822	1.00	11.23	A
ATOM	51	N	VAL	A	149	9.195	6.152	42.192	1.00	10.14	A
ATOM	52	CA	VAL	A	149	8.650	7.027	41.154	1.00	9.36	A
ATOM	53	CB	VAL	A	149	7.099	6.991	41.177	1.00	8.62	A
ATOM	54	CG1	VAL	A	149	6.523	7.938	40.130	1.00	6.99	A
ATOM	55	CG2	VAL	A	149	6.617	5.553	40.929	1.00	5.19	A
ATOM	56	C	VAL	A	149	9.186	8.421	41.493	1.00	10.37	A
ATOM	57	O	VAL	A	149	8.677	9.099	42.392	1.00	12.43	A
ATOM	58	N	CYS	A	150	10.207	8.844	40.757	1.00	8.87	A
ATOM	59	CA	CYS	A	150	10.890	10.108	41.027	1.00	9.53	A
ATOM	60	CB	CYS	A	150	12.389	9.812	41.159	1.00	7.66	A
ATOM	61	SG	CYS	A	150	13.406	11.182	41.672	1.00	8.78	A
ATOM	62	C	CYS	A	150	10.678	11.283	40.073	1.00	8.89	A
ATOM	63	O	CYS	A	150	11.035	11.229	38.895	1.00	10.33	A
ATOM	64	N	ASP	A	151	10.115	12.356	40.618	1.00	9.37	A
ATOM	65	CA	ASP	A	151	9.822	13.591	39.890	1.00	9.11	A
ATOM	66	CB	ASP	A	151	9.110	14.552	40.840	1.00	11.54	A
ATOM	67	CG	ASP	A	151	8.410	15.689	40.129	1.00	11.85	A
ATOM	68	OD1	ASP	A	151	8.906	16.171	39.091	1.00	14.28	A
ATOM	69	OD2	ASP	A	151	7.357	16.113	40.634	1.00	12.34	A
ATOM	70	C	ASP	A	151	11.105	14.256	39.356	1.00	10.14	A
ATOM	71	O	ASP	A	151	12.012	14.575	40.120	1.00	8.58	A
ATOM	72	N	GLU	A	152	11.176	14.470	38.045	1.00	9.69	A
ATOM	73	CA	GLU	A	152	12.349	15.100	37.454	1.00	10.74	A
ATOM	74	CB	GLU	A	152	13.097	14.106	36.548	1.00	12.08	A
ATOM	75	CG	GLU	A	152	12.376	13.735	35.251	1.00	12.78	A
ATOM	76	CD	GLU	A	152	13.161	12.738	34.402	1.00	13.97	A
ATOM	77	OE1	GLU	A	152	14.400	12.675	34.534	1.00	12.78	A
ATOM	78	OE2	GLU	A	152	12.540	12.024	33.588	1.00	14.91	A
ATOM	79	C	GLU	A	152	11.949	16.344	36.661	1.00	11.12	A
ATOM	80	O	GLU	A	152	12.709	16.830	35.823	1.00	11.48	A
ATOM	81	N	SER	A	153	10.758	16.865	36.942	1.00	10.14	A
ATOM	82	CA	SER	A	153	10.266	18.048	36.252	1.00	9.70	A
ATOM	83	CB	SER	A	153	8.803	18.306	36.624	1.00	10.82	A
ATOM	84	OG	SER	A	153	8.654	18.418	38.025	1.00	7.53	A
ATOM	85	C	SER	A	153	11.128	19.264	36.589	1.00	10.23	A
ATOM	86	O	SER	A	153	11.912	19.235	37.539	1.00	10.08	A
ATOM	87	N	ASN	A	154	10.976	20.327	35.801	1.00	8.89	A

ATOM	88	CA	ASN	A	154	11.760	21.548	35.973	1.00	9.70	A
ATOM	89	CB	ASN	A	154	11.320	22.621	34.959	1.00	9.07	A
ATOM	90	CG	ASN	A	154	11.755	22.300	33.524	1.00	12.54	A
ATOM	91	OD1	ASN	A	154	12.534	21.373	33.284	1.00	13.50	A
ATOM	92	ND2	ASN	A	154	11.262	23.084	32.568	1.00	11.08	A
ATOM	93	C	ASN	A	154	11.713	22.144	37.369	1.00	9.06	A
ATOM	94	O	ASN	A	154	12.723	22.629	37.870	1.00	7.54	A
ATOM	95	N	SER	A	155	10.539	22.093	37.997	1.00	10.29	A
ATOM	96	CA	SER	A	155	10.352	22.672	39.327	1.00	9.98	A
ATOM	97	CB	SER	A	155	8.874	22.642	39.710	1.00	9.88	A
ATOM	98	OG	SER	A	155	8.513	21.362	40.193	1.00	11.38	A
ATOM	99	C	SER	A	155	11.159	22.002	40.435	1.00	10.21	A
ATOM	100	O	SER	A	155	11.381	22.601	41.483	1.00	9.99	A
ATOM	101	N	ILE	A	156	11.595	20.766	40.211	1.00	9.91	A
ATOM	102	CA	ILE	A	156	12.364	20.047	41.219	1.00	9.61	A
ATOM	103	CB	ILE	A	156	12.462	18.546	40.861	1.00	8.85	A
ATOM	104	CG2	ILE	A	156	13.467	17.846	41.775	1.00	8.95	A
ATOM	105	CG1	ILE	A	156	11.070	17.898	40.980	1.00	8.39	A
ATOM	106	CD1	ILE	A	156	10.482	17.937	42.394	1.00	2.79	A
ATOM	107	C	ILE	A	156	13.761	20.647	41.406	1.00	9.78	A
ATOM	108	O	ILE	A	156	14.466	20.922	40.439	1.00	9.93	A
ATOM	109	N	TYR	A	157	14.140	20.849	42.667	1.00	8.74	A
ATOM	110	CA	TYR	A	157	15.426	21.448	43.028	1.00	9.40	A
ATOM	111	CB	TYR	A	157	15.376	22.955	42.766	1.00	13.35	A
ATOM	112	CG	TYR	A	157	16.677	23.689	43.009	1.00	14.09	A
ATOM	113	CD1	TYR	A	157	17.557	23.943	41.964	1.00	14.70	A
ATOM	114	CE1	TYR	A	157	18.757	24.621	42.182	1.00	15.23	A
ATOM	115	CD2	TYR	A	157	17.026	24.127	44.289	1.00	15.58	A
ATOM	116	CE2	TYR	A	157	18.222	24.802	44.520	1.00	14.41	A
ATOM	117	CZ	TYR	A	157	19.080	25.047	43.465	1.00	15.28	A
ATOM	118	OH	TYR	A	157	20.258	25.725	43.687	1.00	14.42	A
ATOM	119	C	TYR	A	157	15.662	21.217	44.523	1.00	9.98	A
ATOM	120	O	TYR	A	157	14.727	21.322	45.318	1.00	8.35	A
ATOM	121	N	CPR	A	158	16.903	20.875	44.924	1.00	10.14	A
ATOM	122	CD	CPR	A	158	17.241	20.924	46.358	1.00	8.97	A
ATOM	123	CA	CPR	A	158	18.121	20.678	44.124	1.00	11.99	A
ATOM	124	CB	CPR	A	158	19.218	21.139	45.071	1.00	10.42	A
ATOM	125	CG	CPR	A	158	18.726	20.604	46.372	1.00	10.37	A
ATOM	126	C	CPR	A	158	18.256	19.195	43.781	1.00	11.98	A
ATOM	127	O	CPR	A	158	17.978	18.347	44.618	1.00	13.30	A
ATOM	128	N	TRP	A	159	18.695	18.879	42.569	1.00	13.37	A
ATOM	129	CA	TRP	A	159	18.816	17.481	42.177	1.00	14.62	A
ATOM	130	CB	TRP	A	159	19.273	17.364	40.716	1.00	13.17	A
ATOM	131	CG	TRP	A	159	19.038	16.001	40.141	1.00	12.86	A
ATOM	132	CD2	TRP	A	159	17.773	15.328	40.002	1.00	12.49	A
ATOM	133	CE2	TRP	A	159	18.039	14.052	39.453	1.00	12.27	A
ATOM	134	CE3	TRP	A	159	16.447	15.680	40.286	1.00	12.37	A
ATOM	135	CD1	TRP	A	159	19.982	15.135	39.682	1.00	11.66	A
ATOM	136	NE1	TRP	A	159	19.391	13.960	39.269	1.00	10.69	A
ATOM	137	CZ2	TRP	A	159	17.022	13.122	39.183	1.00	12.98	A
ATOM	138	CZ3	TRP	A	159	15.433	14.755	40.019	1.00	12.83	A
ATOM	139	CH2	TRP	A	159	15.731	13.490	39.471	1.00	12.43	A
ATOM	140	C	TRP	A	159	19.760	16.713	43.098	1.00	14.85	A
ATOM	141	O	TRP	A	159	19.552	15.530	43.352	1.00	16.17	A
ATOM	142	N	ASP	A	160	20.789	17.388	43.603	1.00	15.74	A
ATOM	143	CA	ASP	A	160	21.748	16.761	44.514	1.00	17.53	A

ATOM	144	CB	ASP	A	160	22.715	17.808	45.077	1.00	20.00	A
ATOM	145	CG	ASP	A	160	23.797	18.194	44.090	1.00	25.18	A
ATOM	146	OD1	ASP	A	160	24.384	19.282	44.269	1.00	28.54	A
ATOM	147	OD2	ASP	A	160	24.071	17.414	43.148	1.00	25.23	A
ATOM	148	C	ASP	A	160	21.029	16.077	45.676	1.00	15.95	A
ATOM	149	O	ASP	A	160	21.381	14.967	46.065	1.00	14.81	A
ATOM	150	N	ALA	A	161	20.032	16.757	46.232	1.00	13.82	A
ATOM	151	CA	ALA	A	161	19.265	16.213	47.342	1.00	13.97	A
ATOM	152	CB	ALA	A	161	18.284	17.260	47.863	1.00	13.79	A
ATOM	153	C	ALA	A	161	18.513	14.963	46.897	1.00	13.98	A
ATOM	154	O	ALA	A	161	18.370	14.005	47.660	1.00	13.02	A
ATOM	155	N	VAL	A	162	18.033	14.973	45.658	1.00	14.83	A
ATOM	156	CA	VAL	A	162	17.303	13.826	45.128	1.00	14.59	A
ATOM	157	CB	VAL	A	162	16.614	14.190	43.794	1.00	15.34	A
ATOM	158	CG1	VAL	A	162	15.829	12.991	43.254	1.00	14.23	A
ATOM	159	CG2	VAL	A	162	15.679	15.372	44.011	1.00	13.44	A
ATOM	160	C	VAL	A	162	18.236	12.621	44.934	1.00	14.98	A
ATOM	161	O	VAL	A	162	17.923	11.511	45.365	1.00	15.96	A
ATOM	162	N	LYS	A	163	19.380	12.840	44.290	1.00	15.39	A
ATOM	163	CA	LYS	A	163	20.347	11.764	44.074	1.00	15.08	A
ATOM	164	CB	LYS	A	163	21.593	12.289	43.358	1.00	18.00	A
ATOM	165	CG	LYS	A	163	21.405	12.638	41.892	1.00	21.39	A
ATOM	166	CD	LYS	A	163	22.710	13.194	41.333	1.00	24.66	A
ATOM	167	CE	LYS	A	163	22.648	13.384	39.837	1.00	26.80	A
ATOM	168	NZ	LYS	A	163	23.850	14.103	39.348	1.00	29.83	A
ATOM	169	C	LYS	A	163	20.781	11.158	45.409	1.00	14.49	A
ATOM	170	O	LYS	A	163	20.870	9.936	45.553	1.00	11.86	A
ATOM	171	N	ASN	A	164	21.067	12.020	46.380	1.00	13.30	A
ATOM	172	CA	ASN	A	164	21.494	11.555	47.691	1.00	13.86	A
ATOM	173	CB	ASN	A	164	21.719	12.731	48.633	1.00	13.54	A
ATOM	174	CG	ASN	A	164	22.110	12.286	50.018	1.00	13.56	A
ATOM	175	OD1	ASN	A	164	21.273	12.193	50.918	1.00	12.49	A
ATOM	176	ND2	ASN	A	164	23.386	11.985	50.195	1.00	13.32	A
ATOM	177	C	ASN	A	164	20.462	10.618	48.296	1.00	14.39	A
ATOM	178	O	ASN	A	164	20.797	9.564	48.847	1.00	14.01	A
ATOM	179	N	PHE	A	165	19.201	11.013	48.194	1.00	14.20	A
ATOM	180	CA	PHE	A	165	18.123	10.202	48.721	1.00	13.04	A
ATOM	181	CB	PHE	A	165	16.785	10.899	48.509	1.00	12.24	A
ATOM	182	CG	PHE	A	165	15.613	10.061	48.911	1.00	11.89	A
ATOM	183	CD1	PHE	A	165	15.289	9.896	50.250	1.00	12.66	A
ATOM	184	CD2	PHE	A	165	14.882	9.370	47.954	1.00	12.19	A
ATOM	185	CE1	PHE	A	165	14.251	9.050	50.630	1.00	12.76	A
ATOM	186	CE2	PHE	A	165	13.848	8.524	48.323	1.00	12.35	A
ATOM	187	CZ	PHE	A	165	13.536	8.363	49.664	1.00	11.87	A
ATOM	188	C	PHE	A	165	18.093	8.835	48.036	1.00	13.02	A
ATOM	189	O	PHE	A	165	18.173	7.808	48.695	1.00	14.50	A
ATOM	190	N	LEU	A	166	17.975	8.834	46.711	1.00	13.00	A
ATOM	191	CA	LEU	A	166	17.925	7.594	45.937	1.00	13.67	A
ATOM	192	CB	LEU	A	166	18.004	7.911	44.445	1.00	12.12	A
ATOM	193	CG	LEU	A	166	16.904	8.863	43.968	1.00	12.57	A
ATOM	194	CD1	LEU	A	166	17.103	9.207	42.508	1.00	9.74	A
ATOM	195	CD2	LEU	A	166	15.552	8.217	44.203	1.00	11.27	A
ATOM	196	C	LEU	A	166	19.077	6.681	46.319	1.00	14.74	A
ATOM	197	O	LEU	A	166	18.899	5.488	46.561	1.00	15.55	A
ATOM	198	N	GLU	A	167	20.260	7.277	46.357	1.00	15.63	A
ATOM	199	CA	GLU	A	167	21.496	6.606	46.700	1.00	17.13	A

ATOM	200	CB	GLU	A	167	22.623	7.637	46.626	1.00	20.43	A
ATOM	201	CG	GLU	A	167	24.034	7.105	46.610	1.00	25.09	A
ATOM	202	CD	GLU	A	167	24.977	8.066	45.899	1.00	28.66	A
ATOM	203	OE1	GLU	A	167	26.207	7.859	45.974	1.00	31.85	A
ATOM	204	OE2	GLU	A	167	24.482	9.024	45.254	1.00	29.06	A
ATOM	205	C	GLU	A	167	21.410	5.993	48.095	1.00	16.74	A
ATOM	206	O	GLU	A	167	21.658	4.802	48.265	1.00	16.83	A
ATOM	207	N	LYS	A	168	21.053	6.814	49.084	1.00	16.30	A
ATOM	208	CA	LYS	A	168	20.936	6.373	50.480	1.00	15.74	A
ATOM	209	CB	LYS	A	168	20.725	7.580	51.406	1.00	13.90	A
ATOM	210	CG	LYS	A	168	21.932	8.493	51.548	1.00	14.49	A
ATOM	211	CD	LYS	A	168	23.035	7.809	52.330	1.00	15.70	A
ATOM	212	CE	LYS	A	168	24.143	8.773	52.698	1.00	16.32	A
ATOM	213	NZ	LYS	A	168	24.818	9.345	51.512	1.00	14.90	A
ATOM	214	C	LYS	A	168	19.795	5.379	50.698	1.00	15.80	A
ATOM	215	O	LYS	A	168	19.860	4.528	51.586	1.00	15.98	A
ATOM	216	N	PHE	A	169	18.744	5.506	49.897	1.00	15.19	A
ATOM	217	CA	PHE	A	169	17.602	4.615	50.011	1.00	15.65	A
ATOM	218	CB	PHE	A	169	16.452	5.097	49.112	1.00	12.98	A
ATOM	219	CG	PHE	A	169	15.290	4.146	49.059	1.00	12.73	A
ATOM	220	CD1	PHE	A	169	14.530	3.892	50.192	1.00	12.13	A
ATOM	221	CD2	PHE	A	169	14.988	3.465	47.886	1.00	13.61	A
ATOM	222	CE1	PHE	A	169	13.485	2.971	50.158	1.00	14.03	A
ATOM	223	CE2	PHE	A	169	13.943	2.542	47.846	1.00	13.89	A
ATOM	224	CZ	PHE	A	169	13.193	2.294	48.983	1.00	12.36	A
ATOM	225	C	PHE	A	169	18.022	3.198	49.618	1.00	16.17	A
ATOM	226	O	PHE	A	169	17.779	2.245	50.354	1.00	15.90	A
ATOM	227	N	VAL	A	170	18.664	3.066	48.462	1.00	17.23	A
ATOM	228	CA	VAL	A	170	19.112	1.762	47.984	1.00	18.56	A
ATOM	229	CB	VAL	A	170	19.707	1.881	46.553	1.00	18.42	A
ATOM	230	CG1	VAL	A	170	20.408	0.591	46.154	1.00	17.54	A
ATOM	231	CG2	VAL	A	170	18.593	2.199	45.560	1.00	17.05	A
ATOM	232	C	VAL	A	170	20.148	1.132	48.926	1.00	20.05	A
ATOM	233	O	VAL	A	170	20.217	-0.090	49.058	1.00	20.58	A
ATOM	234	N	GLN	A	171	20.942	1.971	49.584	1.00	21.43	A
ATOM	235	CA	GLN	A	171	21.973	1.504	50.511	1.00	22.80	A
ATOM	236	CB	GLN	A	171	22.786	2.697	51.034	1.00	25.64	A
ATOM	237	CG	GLN	A	171	24.255	2.721	50.617	1.00	27.27	A
ATOM	238	CD	GLN	A	171	25.057	1.580	51.214	1.00	29.69	A
ATOM	239	OE1	GLN	A	171	25.020	1.346	52.423	1.00	31.25	A
ATOM	240	NE2	GLN	A	171	25.794	0.864	50.367	1.00	29.08	A
ATOM	241	C	GLN	A	171	21.389	0.736	51.698	1.00	22.06	A
ATOM	242	O	GLN	A	171	21.986	-0.227	52.182	1.00	19.91	A
ATOM	243	N	GLY	A	172	20.219	1.158	52.162	1.00	22.43	A
ATOM	244	CA	GLY	A	172	19.604	0.498	53.301	1.00	21.98	A
ATOM	245	C	GLY	A	172	18.805	-0.749	52.975	1.00	22.83	A
ATOM	246	O	GLY	A	172	18.207	-1.361	53.862	1.00	21.01	A
ATOM	247	N	LEU	A	173	18.797	-1.141	51.706	1.00	22.94	A
ATOM	248	CA	LEU	A	173	18.041	-2.315	51.304	1.00	23.99	A
ATOM	249	CB	LEU	A	173	17.292	-2.041	50.000	1.00	22.59	A
ATOM	250	CG	LEU	A	173	16.303	-0.875	49.986	1.00	21.28	A
ATOM	251	CD1	LEU	A	173	15.742	-0.728	48.580	1.00	21.16	A
ATOM	252	CD2	LEU	A	173	15.186	-1.109	51.000	1.00	17.99	A
ATOM	253	C	LEU	A	173	18.903	-3.555	51.132	1.00	25.00	A
ATOM	254	O	LEU	A	173	20.073	-3.471	50.772	1.00	23.71	A
ATOM	255	N	ASP	A	174	18.303	-4.707	51.407	1.00	27.54	A

```
ATOM    256  CA  ASP A 174      18.973  -5.993  51.264  1.00 30.47      A
ATOM    257  CB  ASP A 174      18.435  -6.980  52.299  1.00 33.48      A
ATOM    258  CG  ASP A 174      19.424  -8.072  52.630  1.00 37.17      A
ATOM    259  OD1 ASP A 174      20.025  -8.635  51.691  1.00 38.86      A
ATOM    260  OD2 ASP A 174      19.597  -8.372  53.831  1.00 38.36      A
ATOM    261  C   ASP A 174      18.590  -6.451  49.858  1.00 30.22      A
ATOM    262  O   ASP A 174      17.644  -7.216  49.677  1.00 29.33      A
ATOM    263  N   ILE A 175      19.328  -5.957  48.870  1.00 30.40      A
ATOM    264  CA  ILE A 175      19.066  -6.258  47.467  1.00 31.71      A
ATOM    265  CB  ILE A 175      20.031  -5.453  46.570  1.00 31.30      A
ATOM    266  CG2 ILE A 175      19.507  -5.383  45.148  1.00 30.95      A
ATOM    267  CG1 ILE A 175      20.155  -4.027  47.112  1.00 31.50      A
ATOM    268  CD1 ILE A 175      18.828  -3.300  47.254  1.00 31.58      A
ATOM    269  C   ILE A 175      19.146  -7.747  47.123  1.00 32.27      A
ATOM    270  O   ILE A 175      19.241  -8.594  48.009  1.00 33.75      A
ATOM    271  N   GLY A 176      19.089  -8.056  45.831  1.00 32.64      A
ATOM    272  CA  GLY A 176      19.143  -9.437  45.386  1.00 32.16      A
ATOM    273  C   GLY A 176      17.826  -9.910  44.790  1.00 31.98      A
ATOM    274  O   GLY A 176      16.761  -9.471  45.222  1.00 31.33      A
ATOM    275  N   PRO A 177      17.866 -10.796  43.779  1.00 32.34      A
ATOM    276  CD  PRO A 177      19.062 -11.093  42.969  1.00 32.81      A
ATOM    277  CA  PRO A 177      16.664 -11.328  43.126  1.00 32.50      A
ATOM    278  CB  PRO A 177      17.237 -12.152  41.977  1.00 31.55      A
ATOM    279  CG  PRO A 177      18.462 -11.390  41.612  1.00 32.20      A
ATOM    280  C   PRO A 177      15.762 -12.167  44.035  1.00 32.37      A
ATOM    281  O   PRO A 177      14.625 -12.478  43.673  1.00 33.30      A
ATOM    282  N   THR A 178      16.267 -12.536  45.209  1.00 32.01      A
ATOM    283  CA  THR A 178      15.493 -13.342  46.150  1.00 30.96      A
ATOM    284  CB  THR A 178      16.220 -14.650  46.484  1.00 30.93      A
ATOM    285  OG1 THR A 178      17.517 -14.355  47.019  1.00 29.20      A
ATOM    286  CG2 THR A 178      16.363 -15.498  45.235  1.00 30.68      A
ATOM    287  C   THR A 178      15.213 -12.599  47.448  1.00 30.22      A
ATOM    288  O   THR A 178      14.569 -13.126  48.355  1.00 31.00      A
ATOM    289  N   LYS A 179      15.710 -11.372  47.536  1.00 28.83      A
ATOM    290  CA  LYS A 179      15.500 -10.549  48.716  1.00 27.14      A
ATOM    291  CB  LYS A 179      16.849 -10.160  49.321  1.00 27.31      A
ATOM    292  CG  LYS A 179      17.589 -11.369  49.871  1.00 27.60      A
ATOM    293  CD  LYS A 179      18.955 -11.561  49.240  1.00 27.00      A
ATOM    294  CE  LYS A 179      20.026 -10.827  50.025  1.00 28.86      A
ATOM    295  NZ  LYS A 179      21.395 -11.054  49.489  1.00 30.25      A
ATOM    296  C   LYS A 179      14.692  -9.331  48.287  1.00 25.60      A
ATOM    297  O   LYS A 179      13.507  -9.463  48.000  1.00 24.62      A
ATOM    298  N   THR A 180      15.314  -8.157  48.221  1.00 23.79      A
ATOM    299  CA  THR A 180      14.580  -6.966  47.795  1.00 22.88      A
ATOM    300  CB  THR A 180      14.745  -5.798  48.790  1.00 22.04      A
ATOM    301  OG1 THR A 180      14.234  -6.182  50.070  1.00 23.16      A
ATOM    302  CG2 THR A 180      13.979  -4.576  48.304  1.00 20.65      A
ATOM    303  C   THR A 180      15.002  -6.473  46.414  1.00 21.26      A
ATOM    304  O   THR A 180      16.191  -6.322  46.130  1.00 21.51      A
ATOM    305  N   GLN A 181      14.018  -6.225  45.558  1.00 20.39      A
ATOM    306  CA  GLN A 181      14.282  -5.722  44.215  1.00 19.27      A
ATOM    307  CB  GLN A 181      13.526  -6.552  43.173  1.00 19.23      A
ATOM    308  CG  GLN A 181      14.235  -7.832  42.766  1.00 21.63      A
ATOM    309  CD  GLN A 181      13.460  -8.635  41.738  1.00 22.21      A
ATOM    310  OE1 GLN A 181      14.044  -9.370  40.946  1.00 25.69      A
ATOM    311  NE2 GLN A 181      12.139  -8.506  41.750  1.00 22.55      A
```

ATOM	312	C.	GLN	A	181	13.836	-4.262	44.150	1.00	18.57	A
ATOM	313	O	GLN	A	181	12.885	-3.870	44.829	1.00	17.74	A
ATOM	314	N	VAL	A	182	14.522	-3.466	43.333	1.00	17.44	A
ATOM	315	CA	VAL	A	182	14.201	-2.048	43.194	1.00	15.50	A
ATOM	316	CB	VAL	A	182	15.244	-1.160	43.911	1.00	15.13	A
ATOM	317	CG1	VAL	A	182	14.778	0.284	43.913	1.00	15.79	A
ATOM	318	CG2	VAL	A	182	15.482	-1.649	45.322	1.00	16.85	A
ATOM	319	C	VAL	A	182	14.149	-1.584	41.737	1.00	15.79	A
ATOM	320	O	VAL	A	182	15.072	-1.831	40.961	1.00	13.82	A
ATOM	321	N	GLY	A	183	13.062	-0.910	41.375	1.00	14.94	A
ATOM	322	CA	GLY	A	183	12.928	-0.375	40.032	1.00	14.95	A
ATOM	323	C	GLY	A	183	12.910	1.139	40.170	1.00	14.43	A
ATOM	324	O	GLY	A	183	12.498	1.646	41.211	1.00	14.17	A
ATOM	325	N	LEU	A	184	13.355	1.870	39.150	1.00	13.48	A
ATOM	326	CA	LEU	A	184	13.367	3.331	39.227	1.00	12.24	A
ATOM	327	CB	LEU	A	184	14.798	3.846	39.406	1.00	11.95	A
ATOM	328	CG	LEU	A	184	15.071	5.230	40.027	1.00	14.19	A
ATOM	329	CD1	LEU	A	184	16.134	5.930	39.198	1.00	14.35	A
ATOM	330	CD2	LEU	A	184	13.816	6.088	40.098	1.00	13.28	A
ATOM	331	C	LEU	A	184	12.745	3.986	37.993	1.00	11.99	A
ATOM	332	O	LEU	A	184	13.199	3.790	36.866	1.00	12.60	A
ATOM	333	N	ILE	A	185	11.693	4.758	38.221	1.00	11.44	A
ATOM	334	CA	ILE	A	185	10.998	5.473	37.158	1.00	11.08	A
ATOM	335	CB	ILE	A	185	9.489	5.055	37.103	1.00	10.82	A
ATOM	336	CG2	ILE	A	185	8.675	6.068	36.323	1.00	10.02	A
ATOM	337	CG1	ILE	A	185	9.331	3.686	36.430	1.00	12.56	A
ATOM	338	CD1	ILE	A	185	10.111	2.547	37.081	1.00	12.60	A
ATOM	339	C	ILE	A	185	11.125	6.968	37.473	1.00	11.40	A
ATOM	340	O	ILE	A	185	11.068	7.363	38.634	1.00	11.46	A
ATOM	341	N	GLN	A	186	11.345	7.787	36.446	1.00	12.56	A
ATOM	342	CA	GLN	A	186	11.438	9.236	36.623	1.00	11.76	A
ATOM	343	CB	GLN	A	186	12.859	9.726	36.333	1.00	12.89	A
ATOM	344	CG	GLN	A	186	13.867	9.145	37.316	1.00	14.23	A
ATOM	345	CD	GLN	A	186	15.273	9.716	37.197	1.00	15.38	A
ATOM	346	OE1	GLN	A	186	16.206	9.170	37.771	1.00	15.74	A
ATOM	347	NE2	GLN	A	186	15.426	10.819	36.466	1.00	17.29	A
ATOM	348	C	GLN	A	186	10.397	9.886	35.701	1.00	10.97	A
ATOM	349	O	GLN	A	186	10.150	9.404	34.593	1.00	9.90	A
ATOM	350	N	TYR	A	187	9.785	10.973	36.158	1.00	9.31	A
ATOM	351	CA	TYR	A	187	8.718	11.603	35.383	1.00	8.51	A
ATOM	352	CB	TYR	A	187	7.374	11.059	35.880	1.00	8.10	A
ATOM	353	CG	TYR	A	187	6.958	11.613	37.238	1.00	6.73	A
ATOM	354	CD1	TYR	A	187	6.284	12.833	37.339	1.00	6.75	A
ATOM	355	CE1	TYR	A	187	5.938	13.373	38.579	1.00	6.68	A
ATOM	356	CD2	TYR	A	187	7.274	10.939	38.418	1.00	7.94	A
ATOM	357	CE2	TYR	A	187	6.932	11.468	39.671	1.00	9.48	A
ATOM	358	CZ	TYR	A	187	6.267	12.685	39.742	1.00	9.10	A
ATOM	359	OH	TYR	A	187	5.930	13.210	40.974	1.00	12.69	A
ATOM	360	C	TYR	A	187	8.622	13.126	35.348	1.00	7.79	A
ATOM	361	O	TYR	A	187	9.178	13.833	36.177	1.00	8.04	A
ATOM	362	N	ALA	A	188	7.865	13.600	34.367	1.00	8.62	A
ATOM	363	CA	ALA	A	188	7.580	15.011	34.155	1.00	9.11	A
ATOM	364	CB	ALA	A	188	8.734	15.698	33.428	1.00	9.39	A
ATOM	365	C	ALA	A	188	6.323	14.985	33.290	1.00	8.41	A
ATOM	366	O	ALA	A	188	5.259	14.580	33.760	1.00	7.15	A
ATOM	367	N	ASN	A	189	6.434	15.386	32.027	1.00	9.04	A

ATOM	368	CA	ASN	A	189	5.265	15.349	31.155	1.00	10.71	A
ATOM	369	CB	ASN	A	189	5.574	15.979	29.785	1.00	11.19	A
ATOM	370	CG	ASN	A	189	6.067	17.408	29.899	1.00	9.44	A
ATOM	371	OD1	ASN	A	189	5.596	18.301	29.192	1.00	10.99	A
ATOM	372	ND2	ASN	A	189	7.024	17.631	30.783	1.00	7.94	A
ATOM	373	C	ASN	A	189	4.870	13.886	30.978	1.00	10.65	A
ATOM	374	O	ASN	A	189	3.688	13.550	30.898	1.00	10.97	A
ATOM	375	N	ASN	A	190	5.877	13.020	30.957	1.00	11.36	A
ATOM	376	CA	ASN	A	190	5.672	11.590	30.776	1.00	14.30	A
ATOM	377	CB	ASN	A	190	5.913	11.225	29.307	1.00	16.54	A
ATOM	378	CG	ASN	A	190	5.100	12.079	28.357	1.00	17.94	A
ATOM	379	OD1	ASN	A	190	3.880	11.970	28.302	1.00	22.49	A
ATOM	380	ND2	ASN	A	190	5.773	12.945	27.611	1.00	20.09	A
ATOM	381	C	ASN	A	190	6.626	10.785	31.661	1.00	14.69	A
ATOM	382	O	ASN	A	190	7.659	11.287	32.094	1.00	15.45	A
ATOM	383	N	PRO	A	191	6.276	9.527	31.959	1.00	14.55	A
ATOM	384	CD	PRO	A	191	4.934	8.922	31.852	1.00	15.09	A
ATOM	385	CA	PRO	A	191	7.157	8.705	32.795	1.00	14.77	A
ATOM	386	CB	PRO	A	191	6.179	7.780	33.506	1.00	15.27	A
ATOM	387	CG	PRO	A	191	5.153	7.532	32.434	1.00	14.75	A
ATOM	388	C	PRO	A	191	8.167	7.927	31.944	1.00	14.27	A
ATOM	389	O	PRO	A	191	7.879	7.576	30.800	1.00	12.84	A
ATOM	390	N	ARG	A	192	9.347	7.675	32.502	1.00	14.02	A
ATOM	391	CA	ARG	A	192	10.386	6.912	31.807	1.00	14.71	A
ATOM	392	CB	ARG	A	192	11.442	7.842	31.188	1.00	15.69	A
ATOM	393	CG	ARG	A	192	12.396	8.499	32.178	1.00	17.79	A
ATOM	394	CD	ARG	A	192	13.298	9.518	31.477	1.00	18.65	A
ATOM	395	NE	ARG	A	192	14.250	10.148	32.393	1.00	18.93	A
ATOM	396	CZ	ARG	A	192	15.453	9.663	32.684	1.00	17.67	A
ATOM	397	NH1	ARG	A	192	15.868	8.535	32.127	1.00	18.74	A
ATOM	398	NH2	ARG	A	192	16.241	10.304	33.540	1.00	16.64	A
ATOM	399	C	ARG	A	192	11.062	5.941	32.766	1.00	13.25	A
ATOM	400	O	ARG	A	192	11.181	6.205	33.968	1.00	12.96	A
ATOM	401	N	VAL	A	193	11.510	4.819	32.220	1.00	12.65	A
ATOM	402	CA	VAL	A	193	12.171	3.783	32.997	1.00	10.67	A
ATOM	403	CB	VAL	A	193	11.864	2.386	32.410	1.00	10.91	A
ATOM	404	CG1	VAL	A	193	12.505	1.298	33.264	1.00	11.42	A
ATOM	405	CG2	VAL	A	193	10.364	2.178	32.321	1.00	11.64	A
ATOM	406	C	VAL	A	193	13.690	3.961	33.025	1.00	11.35	A
ATOM	407	O	VAL	A	193	14.331	4.024	31.973	1.00	12.07	A
ATOM	408	N	VAL	A	194	14.257	4.061	34.226	1.00	8.35	A
ATOM	409	CA	VAL	A	194	15.706	4.177	34.378	1.00	8.60	A
ATOM	410	CB	VAL	A	194	16.093	4.934	35.663	1.00	5.55	A
ATOM	411	CG1	VAL	A	194	17.602	5.133	35.716	1.00	5.04	A
ATOM	412	CG2	VAL	A	194	15.393	6.268	35.697	1.00	2.79	A
ATOM	413	C	VAL	A	194	16.179	2.724	34.467	1.00	8.86	A
ATOM	414	O	VAL	A	194	17.158	2.331	33.839	1.00	10.78	A
ATOM	415	N	PHE	A	195	15.465	1.931	35.257	1.00	11.00	A
ATOM	416	CA	PHE	A	195	15.754	0.507	35.386	1.00	13.26	A
ATOM	417	CB	PHE	A	195	17.117	0.259	36.080	1.00	13.43	A
ATOM	418	CG	PHE	A	195	17.210	0.742	37.510	1.00	14.88	A
ATOM	419	CD1	PHE	A	195	16.588	0.049	38.543	1.00	16.46	A
ATOM	420	CD2	PHE	A	195	17.997	1.844	37.831	1.00	15.15	A
ATOM	421	CE1	PHE	A	195	16.756	0.443	39.875	1.00	16.97	A
ATOM	422	CE2	PHE	A	195	18.172	2.245	39.155	1.00	14.80	A
ATOM	423	CZ	PHE	A	195	17.552	1.543	40.180	1.00	16.03	A

ATOM	424	C	PHE	A	195	14:608	-0.180	36.109	1.00 13.40	A
ATOM	425	O	PHE	A	195	13.945	0.435	36.938	1.00 14.78	A
ATOM	426	N	ASN	A	196	14.333	-1.434	35.755	1.00 14.32	A
ATOM	427	CA	ASN	A	196	13.245	-2.179	36.392	1.00 13.90	A
ATOM	428	CB	ASN	A	196	12.531	-3.082	35.378	1.00 15.25	A
ATOM	429	CG	ASN	A	196	11.710	-2.302	34.371	1.00 17.15	A
ATOM	430	OD1	ASN	A	196	11.128	-1.270	34.700	1.00 19.15	A
ATOM	431	ND2	ASN	A	196	11.642	-2.805	33.137	1.00 16.10	A
ATOM	432	C	ASN	A	196	13.737	-3.040	37.549	1.00 13.87	A
ATOM	433	O	ASN	A	196	14.926	-3.048	37.878	1.00 13.98	A
ATOM	434	N	LEU	A	197	12.810	-3.765	38.162	1.00 13.49	A
ATOM	435	CA	LEU	A	197	13.131	-4.655	39.275	1.00 14.75	A
ATOM	436	CB	LEU	A	197	11.855	-5.361	39.768	1.00 12.51	A
ATOM	437	CG	LEU	A	197	10.737	-4.523	40.416	1.00 13.99	A
ATOM	438	CD1	LEU	A	197	9.439	-5.328	40.476	1.00 13.87	A
ATOM	439	CD2	LEU	A	197	11.162	-4.096	41.815	1.00 14.46	A
ATOM	440	C	LEU	A	197	14.128	-5.696	38.776	1.00 15.08	A
ATOM	441	O	LEU	A	197	14.957	-6.197	39.532	1.00 15.32	A
ATOM	442	N	ASN	A	198	14.017	-5.983	37.482	1.00 17.33	A
ATOM	443	CA	ASN	A	198	14.813	-6.963	36.739	1.00 20.71	A
ATOM	444	CB	ASN	A	198	14.026	-7.383	35.493	1.00 21.97	A
ATOM	445	CG	ASN	A	198	13.523	-8.790	35.571	1.00 24.43	A
ATOM	446	OD1	ASN	A	198	12.727	-9.226	34.735	1.00 24.41	A
ATOM	447	ND2	ASN	A	198	13.986	-9.525	36.575	1.00 26.72	A
ATOM	448	C	ASN	A	198	16.200	-6.532	36.261	1.00 21.07	A
ATOM	449	O	ASN	A	198	17.111	-7.353	36.151	1.00 20.61	A
ATOM	450	N	THR	A	199	16.336	-5.252	35.947	1.00 22.19	A
ATOM	451	CA	THR	A	199	17.572	-4.705	35.400	1.00 23.60	A
ATOM	452	CB	THR	A	199	17.479	-3.182	35.299	1.00 22.21	A
ATOM	453	OG1	THR	A	199	16.295	-2.830	34.575	1.00 20.93	A
ATOM	454	CG2	THR	A	199	18.696	-2.628	34.580	1.00 20.97	A
ATOM	455	C	THR	A	199	18.902	-5.048	36.060	1.00 25.62	A
ATOM	456	O	THR	A	199	19.775	-5.637	35.426	1.00 25.51	A
ATOM	457	N	TYR	A	200	19.066	-4.678	37.323	1.00 28.07	A
ATOM	458	CA	TYR	A	200	20.326	-4.929	37.996	1.00 30.24	A
ATOM	459	CB	TYR	A	200	20.790	-3.649	38.695	1.00 29.51	A
ATOM	460	CG	TYR	A	200	21.093	-2.566	37.686	1.00 26.61	A
ATOM	461	CD1	TYR	A	200	20.342	-1.393	37.638	1.00 25.36	A
ATOM	462	CE1	TYR	A	200	20.563	-0.440	36.638	1.00 24.79	A
ATOM	463	CD2	TYR	A	200	22.078	-2.762	36.715	1.00 25.72	A
ATOM	464	CE2	TYR	A	200	22.303	-1.823	35.715	1.00 25.09	A
ATOM	465	CZ	TYR	A	200	21.543	-0.669	35.680	1.00 23.72	A
ATOM	466	OH	TYR	A	200	21.755	0.238	34.671	1.00 24.44	A
ATOM	467	C	TYR	A	200	20.385	-6.118	38.932	1.00 32.84	A
ATOM	468	O	TYR	A	200	19.412	-6.472	39.593	1.00 34.10	A
ATOM	469	N	LYS	A	201	21.566	-6.724	38.964	1.00 35.33	A
ATOM	470	CA	LYS	A	201	21.846	-7.911	39.752	1.00 37.85	A
ATOM	471	CB	LYS	A	201	22.921	-8.736	39.041	1.00 38.62	A
ATOM	472	CG	LYS	A	201	22.840	-8.683	37.511	1.00 40.89	A
ATOM	473	CD	LYS	A	201	23.303	-7.334	36.957	1.00 41.42	A
ATOM	474	CE	LYS	A	201	23.243	-7.290	35.435	1.00 41.97	A
ATOM	475	NZ	LYS	A	201	23.770	-5.999	34.902	1.00 40.92	A
ATOM	476	C	LYS	A	201	22.297	-7.620	41.182	1.00 38.43	A
ATOM	477	O	LYS	A	201	21.700	-8.111	42.141	1.00 38.87	A
ATOM	478	N	THR	A	202	23.353	-6.825	41.323	1.00 39.09	A
ATOM	479	CA	THR	A	202	23.881	-6.506	42.643	1.00 39.33	A

```
ATOM    480  CB  THR A 202      25.406  -6.698  42.692  1.00 39.50      A
ATOM    481  OG1 THR A 202      26.042  -5.675  41.916  1.00 39.36      A
ATOM    482  CG2 THR A 202      25.787  -8.062  42.131  1.00 38.99      A
ATOM    483  C   THR A 202      23.576  -5.092  43.112  1.00 39.86      A
ATOM    484  O   THR A 202      23.195  -4.222  42.328  1.00 40.54      A
ATOM    485  N   LYS A 203      23.766  -4.880  44.408  1.00 39.50      A
ATOM    486  CA  LYS A 203      23.531  -3.598  45.053  1.00 39.14      A
ATOM    487  CB  LYS A 203      23.718  -3.775  46.561  1.00 39.00      A
ATOM    488  CG  LYS A 203      23.223  -2.641  47.432  1.00 38.99      A
ATOM    489  CD  LYS A 203      23.210  -3.101  48.881  1.00 38.85      A
ATOM    490  CE  LYS A 203      22.743  -2.017  49.823  1.00 38.65      A
ATOM    491  NZ  LYS A 203      22.657  -2.540  51.210  1.00 39.40      A
ATOM    492  C   LYS A 203      24.495  -2.540  44.516  1.00 39.51      A
ATOM    493  O   LYS A 203      24.171  -1.350  44.462  1.00 39.55      A
ATOM    494  N   GLU A 204      25.681  -2.990  44.118  1.00 39.07      A
ATOM    495  CA  GLU A 204      26.715  -2.110  43.582  1.00 38.48      A
ATOM    496  CB  GLU A 204      28.023  -2.886  43.406  1.00 38.84      A
ATOM    497  CG  GLU A 204      27.969  -4.318  43.910  1.00 39.73      A
ATOM    498  CD  GLU A 204      27.896  -4.399  45.421  1.00 40.43      A
ATOM    499  OE1 GLU A 204      27.004  -5.107  45.943  1.00 39.63      A
ATOM    500  OE2 GLU A 204      28.740  -3.756  46.085  1.00 41.63      A
ATOM    501  C   GLU A 204      26.295  -1.538  42.234  1.00 37.65      A
ATOM    502  O   GLU A 204      26.323  -0.326  42.019  1.00 37.61      A
ATOM    503  N   GLU A 205      25.917  -2.429  41.326  1.00 36.53      A
ATOM    504  CA  GLU A 205      25.496  -2.043  39.989  1.00 36.06      A
ATOM    505  CB  GLU A 205      25.192  -3.298  39.176  1.00 37.10      A
ATOM    506  CG  GLU A 205      26.288  -4.343  39.278  1.00 39.86      A
ATOM    507  CD  GLU A 205      25.919  -5.646  38.607  1.00 41.30      A
ATOM    508  OE1 GLU A 205      25.768  -5.656  37.368  1.00 42.71      A
ATOM    509  OE2 GLU A 205      25.778  -6.660  39.324  1.00 42.41      A
ATOM    510  C   GLU A 205      24.267  -1.144  40.046  1.00 34.97      A
ATOM    511  O   GLU A 205      23.984  -0.402  39.102  1.00 34.32      A
ATOM    512  N   MET A 206      23.542  -1.209  41.158  1.00 33.42      A
ATOM    513  CA  MET A 206      22.349  -0.396  41.333  1.00 32.37      A
ATOM    514  CB  MET A 206      21.351  -1.094  42.260  1.00 32.31      A
ATOM    515  CG  MET A 206      20.103  -0.266  42.541  1.00 31.24      A
ATOM    516  SD  MET A 206      18.839  -1.174  43.439  1.00 31.05      A
ATOM    517  CE  MET A 206      18.222  -2.247  42.128  1.00 30.66      A
ATOM    518  C   MET A 206      22.694   0.978  41.891  1.00 32.05      A
ATOM    519  O   MET A 206      22.024   1.960  41.576  1.00 32.40      A
ATOM    520  N   ILE A 207      23.726   1.044  42.730  1.00 31.87      A
ATOM    521  CA  ILE A 207      24.159   2.317  43.307  1.00 31.74      A
ATOM    522  CB  ILE A 207      25.070   2.111  44.543  1.00 33.09      A
ATOM    523  CG2 ILE A 207      25.792   3.411  44.893  1.00 32.55      A
ATOM    524  CG1 ILE A 207      24.226   1.642  45.730  1.00 33.77      A
ATOM    525  CD1 ILE A 207      23.174   2.655  46.162  1.00 34.33      A
ATOM    526  C   ILE A 207      24.926   3.092  42.248  1.00 30.68      A
ATOM    527  O   ILE A 207      24.890   4.325  42.210  1.00 29.86      A
ATOM    528  N   VAL A 208      25.623   2.355  41.391  1.00 30.42      A
ATOM    529  CA  VAL A 208      26.381   2.964  40.311  1.00 31.48      A
ATOM    530  CB  VAL A 208      27.281   1.918  39.612  1.00 31.48      A
ATOM    531  CG1 VAL A 208      27.992   2.544  38.432  1.00 32.42      A
ATOM    532  CG2 VAL A 208      28.301   1.369  40.602  1.00 31.32      A
ATOM    533  C   VAL A 208      25.383   3.547  39.305  1.00 32.02      A
ATOM    534  O   VAL A 208      25.626   4.595  38.706  1.00 33.11      A
ATOM    535  N   ALA A 209      24.253   2.869  39.135  1.00 32.28      A
```

ATOM	536	CA	ALA	A	209	23.223	3.329	38.211	1.00	32.70	A
ATOM	537	CB	ALA	A	209	22.272	2.191	37.880	1.00	32.73	A
ATOM	538	C	ALA	A	209	22.451	4.496	38.813	1.00	32.58	A
ATOM	539	O	ALA	A	209	21.990	5.384	38.095	1.00	33.82	A
ATOM	540	N	THR	A	210	22.321	4.488	40.136	1.00	32.14	A
ATOM	541	CA	THR	A	210	21.607	5.535	40.855	1.00	32.31	A
ATOM	542	CB	THR	A	210	21.264	5.069	42.302	1.00	33.35	A
ATOM	543	OG1	THR	A	210	20.037	4.328	42.288	1.00	33.29	A
ATOM	544	CG2	THR	A	210	21.126	6.255	43.243	1.00	33.92	A
ATOM	545	C	THR	A	210	22.400	6.839	40.916	1.00	32.17	A
ATOM	546	O	THR	A	210	21.841	7.925	40.749	1.00	32.64	A
ATOM	547	N	SER	A	211	23.702	6.730	41.153	1.00	30.78	A
ATOM	548	CA	SER	A	211	24.557	7.908	41.247	1.00	29.00	A
ATOM	549	CB	SER	A	211	25.908	7.527	41.856	1.00	28.21	A
ATOM	550	OG	SER	A	211	26.634	6.686	40.979	1.00	27.75	A
ATOM	551	C	SER	A	211	24.784	8.578	39.896	1.00	27.56	A
ATOM	552	O	SER	A	211	25.278	9.697	39.833	1.00	27.13	A
ATOM	553	N	GLN	A	212	24.431	7.892	38.815	1.00	28.19	A
ATOM	554	CA	GLN	A	212	24.613	8.452	37.479	1.00	27.49	A
ATOM	555	CB	GLN	A	212	25.237	7.412	36.544	1.00	30.62	A
ATOM	556	CG	GLN	A	212	26.642	6.967	36.924	1.00	34.70	A
ATOM	557	CD	GLN	A	212	27.162	5.863	36.023	1.00	36.58	A
ATOM	558	OE1	GLN	A	212	27.340	6.057	34.821	1.00	38.55	A
ATOM	559	NE2	GLN	A	212	27.402	4.694	36.599	1.00	38.36	A
ATOM	560	C	GLN	A	212	23.318	8.954	36.849	1.00	25.98	A
ATOM	561	O	GLN	A	212	23.321	9.377	35.692	1.00	26.21	A
ATOM	562	N	THR	A	213	22.210	8.910	37.589	1.00	23.91	A
ATOM	563	CA	THR	A	213	20.937	9.365	37.023	1.00	21.37	A
ATOM	564	CB	THR	A	213	19.722	8.884	37.870	1.00	22.04	A
ATOM	565	OG1	THR	A	213	18.516	9.079	37.118	1.00	20.11	A
ATOM	566	CG2	THR	A	213	19.618	9.662	39.185	1.00	20.81	A
ATOM	567	C	THR	A	213	20.908	10.889	36.884	1.00	19.19	A
ATOM	568	O	THR	A	213	21.407	11.608	37.746	1.00	19.45	A
ATOM	569	N	SER	A	214	20.330	11.371	35.789	1.00	17.46	A
ATOM	570	CA	SER	A	214	20.249	12.809	35.516	1.00	15.88	A
ATOM	571	CB	SER	A	214	20.904	13.102	34.170	1.00	17.30	A
ATOM	572	OG	SER	A	214	20.408	12.205	33.192	1.00	17.87	A
ATOM	573	C	SER	A	214	18.816	13.343	35.500	1.00	13.83	A
ATOM	574	O	SER	A	214	17.867	12.577	35.390	1.00	13.38	A
ATOM	575	N	GLN	A	215	18.669	14.662	35.604	1.00	13.31	A
ATOM	576	CA	GLN	A	215	17.346	15.291	35.599	1.00	11.72	A
ATOM	577	CB	GLN	A	215	17.325	16.517	36.523	1.00	8.11	A
ATOM	578	CG	GLN	A	215	15.926	17.142	36.665	1.00	8.56	A
ATOM	579	CD	GLN	A	215	15.882	18.365	37.572	1.00	8.42	A
ATOM	580	OE1	GLN	A	215	14.814	18.935	37.815	1.00	7.13	A
ATOM	581	NE2	GLN	A	215	17.041	18.775	38.076	1.00	10.20	A
ATOM	582	C	GLN	A	215	16.951	15.720	34.186	1.00	12.51	A
ATOM	583	O	GLN	A	215	17.490	16.687	33.658	1.00	11.99	A
ATOM	584	N	TYR	A	216	16.015	15.008	33.569	1.00	13.04	A
ATOM	585	CA	TYR	A	216	15.602	15.363	32.216	1.00	14.05	A
ATOM	586	CB	TYR	A	216	14.882	14.195	31.536	1.00	15.39	A
ATOM	587	CG	TYR	A	216	15.804	13.142	30.955	1.00	18.06	A
ATOM	588	CD1	TYR	A	216	15.354	12.272	29.966	1.00	19.67	A
ATOM	589	CE1	TYR	A	216	16.192	11.298	29.423	1.00	21.91	A
ATOM	590	CD2	TYR	A	216	17.124	13.013	31.392	1.00	19.95	A
ATOM	591	CE2	TYR	A	216	17.967	12.047	30.859	1.00	20.95	A

ATOM	592	CZ	TYR	A	216	17.493	11.192	29.874	1.00	22.84	A
ATOM	593	OH	TYR	A	216	18.318	10.228	29.341	1.00	26.01	A
ATOM	594	C	TYR	A	216	14.731	16.612	32.113	1.00	14.20	A
ATOM	595	O	TYR	A	216	14.634	17.202	31.042	1.00	13.97	A
ATOM	596	N	GLY	A	217	14.098	17.017	33.211	1.00	13.36	A
ATOM	597	CA	GLY	A	217	13.253	18.201	33.167	1.00	12.97	A
ATOM	598	C	GLY	A	217	11.888	17.993	32.527	1.00	12.66	A
ATOM	599	O	GLY	A	217	11.501	16.870	32.222	1.00	12.59	A
ATOM	600	N	GLY	A	218	11.155	19.087	32.330	1.00	12.62	A
ATOM	601	CA	GLY	A	218	9.830	19.012	31.737	1.00	12.30	A
ATOM	602	C	GLY	A	218	8.964	20.163	32.223	1.00	12.00	A
ATOM	603	O	GLY	A	218	9.017	20.515	33.402	1.00	12.24	A
ATOM	604	N	ASP	A	219	8.164	20.749	31.332	1.00	11.18	A
ATOM	605	CA	ASP	A	219	7.321	21.878	31.709	1.00	10.02	A
ATOM	606	CB	ASP	A	219	7.130	22.830	30.516	1.00	11.41	A
ATOM	607	CG	ASP	A	219	6.441	22.173	29.324	1.00	12.87	A
ATOM	608	OD1	ASP	A	219	6.287	22.858	28.292	1.00	14.29	A
ATOM	609	OD2	ASP	A	219	6.053	20.992	29.406	1.00	12.54	A
ATOM	610	C	ASP	A	219	5.971	21.502	32.312	1.00	9.50	A
ATOM	611	O	ASP	A	219	5.110	22.362	32.522	1.00	7.36	A
ATOM	612	N	LEU	A	220	5.795	20.212	32.587	1.00	9.79	A
ATOM	613	CA	LEU	A	220	4.571	19.696	33.199	1.00	9.49	A
ATOM	614	CB	LEU	A	220	3.662	19.065	32.148	1.00	9.54	A
ATOM	615	CG	LEU	A	220	2.915	19.975	31.180	1.00	11.66	A
ATOM	616	CD1	LEU	A	220	2.134	19.116	30.186	1.00	9.54	A
ATOM	617	CD2	LEU	A	220	1.985	20.892	31.970	1.00	9.87	A
ATOM	618	C	LEU	A	220	4.951	18.629	34.218	1.00	9.13	A
ATOM	619	O	LEU	A	220	5.960	17.957	34.050	1.00	8.03	A
ATOM	620	N	THR	A	221	4.142	18.475	35.265	1.00	9.46	A
ATOM	621	CA	THR	A	221	4.398	17.468	36.301	1.00	8.93	A
ATOM	622	CB	THR	A	221	4.666	18.134	37.666	1.00	8.64	A
ATOM	623	OG1	THR	A	221	5.695	19.117	37.506	1.00	9.50	A
ATOM	624	CG2	THR	A	221	5.119	17.105	38.702	1.00	7.39	A
ATOM	625	C	THR	A	221	3.177	16.559	36.404	1.00	8.53	A
ATOM	626	O	THR	A	221	2.223	16.841	37.135	1.00	8.33	A
ATOM	627	N	ASN	A	222	3.198	15.472	35.647	1.00	8.72	A
ATOM	628	CA	ASN	A	222	2.086	14.536	35.654	1.00	10.94	A
ATOM	629	CB	ASN	A	222	1.851	14.007	34.235	1.00	10.58	A
ATOM	630	CG	ASN	A	222	1.276	15.072	33.302	1.00	9.81	A
ATOM	631	OD1	ASN	A	222	1.610	15.132	32.116	1.00	11.30	A
ATOM	632	ND2	ASN	A	222	0.401	15.907	33.835	1.00	8.55	A
ATOM	633	C	ASN	A	222	2.364	13.399	36.631	1.00	11.86	A
ATOM	634	O	ASN	A	222	2.607	12.261	36.236	1.00	13.30	A
ATOM	635	N	THR	A	223	2.319	13.733	37.916	1.00	12.19	A
ATOM	636	CA	THR	A	223	2.575	12.783	38.993	1.00	12.73	A
ATOM	637	CB	THR	A	223	2.471	13.486	40.370	1.00	13.31	A
ATOM	638	OG1	THR	A	223	3.541	14.429	40.506	1.00	12.62	A
ATOM	639	CG2	THR	A	223	2.537	12.470	41.508	1.00	12.94	A
ATOM	640	C	THR	A	223	1.661	11.563	39.004	1.00	13.25	A
ATOM	641	O	THR	A	223	2.132	10.427	39.102	1.00	14.41	A
ATOM	642	N	PHE	A	224	0.356	11.788	38.904	1.00	11.80	A
ATOM	643	CA	PHE	A	224	-0.579	10.674	38.939	1.00	10.73	A
ATOM	644	CB	PHE	A	224	-1.961	11.199	39.308	1.00	10.15	A
ATOM	645	CG	PHE	A	224	-1.977	11.869	40.644	1.00	8.46	A
ATOM	646	CD1	PHE	A	224	-1.826	13.249	40.750	1.00	6.48	A
ATOM	647	CD2	PHE	A	224	-2.000	11.104	41.811	1.00	8.25	A

ATOM	648	CE1	PHE	A	224	-1.688	13.857	41.995	1.00	4.99	A
ATOM	649	CE2	PHE	A	224	-1.863	11.704	43.058	1.00	8.12	A
ATOM	650	CZ	PHE	A	224	-1.704	13.090	43.148	1.00	5.58	A
ATOM	651	C	PHE	A	224	-0.582	9.820	37.678	1.00	10.20	A
ATOM	652	O	PHE	A	224	-0.927	8.639	37.718	1.00	9.26	A
ATOM	653	N	GLY	A	225	-0.167	10.406	36.563	1.00	10.24	A
ATOM	654	CA	GLY	A	225	-0.079	9.633	35.341	1.00	9.66	A
ATOM	655	C	GLY	A	225	1.059	8.643	35.535	1.00	10.12	A
ATOM	656	O	GLY	A	225	0.958	7.479	35.143	1.00	10.28	A
ATOM	657	N	ALA	A	226	2.143	9.107	36.159	1.00	9.46	A
ATOM	658	CA	ALA	A	226	3.312	8.263	36.426	1.00	8.28	A
ATOM	659	CB	ALA	A	226	4.473	9.119	36.924	1.00	7.03	A
ATOM	660	C	ALA	A	226	3.004	7.169	37.447	1.00	9.17	A
ATOM	661	O	ALA	A	226	3.409	6.013	37.281	1.00	10.19	A
ATOM	662	N	ILE	A	227	2.309	7.541	38.516	1.00	9.78	A
ATOM	663	CA	ILE	A	227	1.941	6.584	39.550	1.00	9.72	A
ATOM	664	CB	ILE	A	227	1.149	7.271	40.688	1.00	10.17	A
ATOM	665	CG2	ILE	A	227	0.449	6.220	41.559	1.00	8.49	A
ATOM	666	CG1	ILE	A	227	2.102	8.141	41.520	1.00	5.96	A
ATOM	667	CD1	ILE	A	227	1.422	8.912	42.637	1.00	4.20	A
ATOM	668	C	ILE	A	227	1.086	5.510	38.901	1.00	10.73	A
ATOM	669	O	ILE	A	227	1.295	4.316	39.119	1.00	9.03	A
ATOM	670	N	GLN	A	228	0.141	5.952	38.077	1.00	13.02	A
ATOM	671	CA	GLN	A	228	-0.755	5.054	37.361	1.00	15.61	A
ATOM	672	CB	GLN	A	228	-1.747	5.880	36.528	1.00	20.26	A
ATOM	673	CG	GLN	A	228	-2.777	5.082	35.738	1.00	22.92	A
ATOM	674	CD	GLN	A	228	-3.870	5.971	35.157	1.00	26.27	A
ATOM	675	OE1	GLN	A	228	-4.806	6.365	35.853	1.00	26.95	A
ATOM	676	NE2	GLN	A	228	-3.745	6.304	33.879	1.00	28.79	A
ATOM	677	C	GLN	A	228	0.046	4.106	36.472	1.00	15.48	A
ATOM	678	O	GLN	A	228	-0.303	2.940	36.338	1.00	14.93	A
ATOM	679	N	TYR	A	229	1.130	4.606	35.883	1.00	17.26	A
ATOM	680	CA	TYR	A	229	1.979	3.794	35.016	1.00	17.37	A
ATOM	681	CB	TYR	A	229	2.998	4.667	34.274	1.00	20.45	A
ATOM	682	CG	TYR	A	229	4.128	3.858	33.669	1.00	21.99	A
ATOM	683	CD1	TYR	A	229	3.983	3.231	32.430	1.00	23.54	A
ATOM	684	CE1	TYR	A	229	4.985	2.394	31.923	1.00	23.85	A
ATOM	685	CD2	TYR	A	229	5.306	3.637	34.385	1.00	24.04	A
ATOM	686	CE2	TYR	A	229	6.311	2.803	33.891	1.00	24.50	A
ATOM	687	CZ	TYR	A	229	6.146	2.183	32.662	1.00	25.44	A
ATOM	688	OH	TYR	A	229	7.140	1.345	32.189	1.00	25.30	A
ATOM	689	C	TYR	A	229	2.734	2.732	35.810	1.00	16.60	A
ATOM	690	O	TYR	A	229	2.780	1.565	35.417	1.00	15.96	A
ATOM	691	N	ALA	A	230	3.338	3.148	36.918	1.00	14.62	A
ATOM	692	CA	ALA	A	230	4.101	2.235	37.760	1.00	14.49	A
ATOM	693	CB	ALA	A	230	4.723	2.993	38.917	1.00	11.62	A
ATOM	694	C	ALA	A	230	3.211	1.109	38.281	1.00	14.68	A
ATOM	695	O	ALA	A	230	3.644	-0.039	38.384	1.00	14.61	A
ATOM	696	N	ARG	A	231	1.968	1.449	38.606	1.00	14.64	A
ATOM	697	CA	ARG	A	231	1.001	0.475	39.099	1.00	16.45	A
ATOM	698	CB	ARG	A	231	-0.317	1.174	39.469	1.00	18.66	A
ATOM	699	CG	ARG	A	231	-1.423	0.214	39.908	1.00	22.57	A
ATOM	700	CD	ARG	A	231	-2.787	0.889	40.034	1.00	24.72	A
ATOM	701	NE	ARG	A	231	-3.701	0.479	38.968	1.00	27.48	A
ATOM	702	CZ	ARG	A	231	-3.796	1.080	37.786	1.00	29.16	A
ATOM	703	NH1	ARG	A	231	-3.039	2.134	37.506	1.00	31.61	A

```
ATOM    704  NH2 ARG A 231      -4.639   0.618  36.875  1.00 28.80      A
ATOM    705  C   ARG A 231       0.720  -0.574  38.027  1.00 16.48      A
ATOM    706  O   ARG A 231       0.720  -1.778  38.295  1.00 16.36      A
ATOM    707  N   LYS A 232       0.491  -0.092  36.809  1.00 16.71      A
ATOM    708  CA  LYS A 232       0.172  -0.929  35.663  1.00 17.22      A
ATOM    709  CB  LYS A 232      -0.400  -0.064  34.536  1.00 19.84      A
ATOM    710  CG  LYS A 232      -1.869  -0.315  34.226  1.00 22.04      A
ATOM    711  CD  LYS A 232      -2.329   0.535  33.048  1.00 24.75      A
ATOM    712  CE  LYS A 232      -3.755   0.200  32.631  1.00 25.02      A
ATOM    713  NZ  LYS A 232      -4.201   1.048  31.488  1.00 25.38      A
ATOM    714  C   LYS A 232       1.293  -1.784  35.087  1.00 17.72      A
ATOM    715  O   LYS A 232       1.034  -2.900  34.635  1.00 17.20      A
ATOM    716  N   TYR A 233       2.528  -1.282  35.101  1.00 17.41      A
ATOM    717  CA  TYR A 233       3.649  -2.024  34.512  1.00 15.33      A
ATOM    718  CB  TYR A 233       4.139  -1.307  33.244  1.00 16.24      A
ATOM    719  CG  TYR A 233       3.065  -1.019  32.218  1.00 16.40      A
ATOM    720  CD1 TYR A 233       2.234   0.091  32.342  1.00 16.16      A
ATOM    721  CE1 TYR A 233       1.233   0.355  31.404  1.00 16.64      A
ATOM    722  CD2 TYR A 233       2.873  -1.867  31.129  1.00 17.49      A
ATOM    723  CE2 TYR A 233       1.879  -1.616  30.185  1.00 18.11      A
ATOM    724  CZ  TYR A 233       1.062  -0.502  30.329  1.00 17.98      A
ATOM    725  OH  TYR A 233       0.083  -0.252  29.395  1.00 18.24      A
ATOM    726  C   TYR A 233       4.879  -2.300  35.377  1.00 14.96      A
ATOM    727  O   TYR A 233       5.531  -3.329  35.212  1.00 13.87      A
ATOM    728  N   ALA A 234       5.213  -1.380  36.275  1.00 14.34      A
ATOM    729  CA  ALA A 234       6.407  -1.524  37.105  1.00 12.68      A
ATOM    730  CB  ALA A 234       6.546  -0.319  38.020  1.00 14.11      A
ATOM    731  C   ALA A 234       6.524  -2.815  37.914  1.00 12.51      A
ATOM    732  O   ALA A 234       7.635  -3.227  38.264  1.00 10.34      A
ATOM    733  N   TYR A 235       5.392  -3.448  38.211  1.00 13.05      A
ATOM    734  CA  TYR A 235       5.388  -4.697  38.976  1.00 13.59      A
ATOM    735  CB  TYR A 235       4.434  -4.600  40.176  1.00 12.71      A
ATOM    736  CG  TYR A 235       4.647  -3.390  41.068  1.00 11.29      A
ATOM    737  CD1 TYR A 235       4.002  -2.179  40.800  1.00  8.56      A
ATOM    738  CE1 TYR A 235       4.206  -1.055  41.605  1.00  8.57      A
ATOM    739  CD2 TYR A 235       5.508  -3.454  42.172  1.00  9.88      A
ATOM    740  CE2 TYR A 235       5.721  -2.337  42.985  1.00  9.49      A
ATOM    741  CZ  TYR A 235       5.067  -1.137  42.697  1.00  9.85      A
ATOM    742  OH  TYR A 235       5.276  -0.031  43.504  1.00  6.17      A
ATOM    743  C   TYR A 235       4.976  -5.899  38.120  1.00 14.95      A
ATOM    744  O   TYR A 235       4.813  -7.005  38.633  1.00 14.95      A
ATOM    745  N   SER A 236       4.803  -5.688  36.819  1.00 15.83      A
ATOM    746  CA  SER A 236       4.406  -6.780  35.937  1.00 16.58      A
ATOM    747  CB  SER A 236       4.101  -6.248  34.537  1.00 15.85      A
ATOM    748  OG  SER A 236       5.278  -5.798  33.897  1.00 15.96      A
ATOM    749  C   SER A 236       5.499  -7.843  35.854  1.00 18.03      A
ATOM    750  O   SER A 236       6.672  -7.570  36.110  1.00 18.46      A
ATOM    751  N   ALA A 237       5.114  -9.063  35.502  1.00 19.89      A
ATOM    752  CA  ALA A 237       6.090 -10.138  35.394  1.00 20.13      A
ATOM    753  CB  ALA A 237       5.401 -11.426  34.961  1.00 21.77      A
ATOM    754  C   ALA A 237       7.192  -9.759  34.399  1.00 19.78      A
ATOM    755  O   ALA A 237       8.356 -10.100  34.598  1.00 20.26      A
ATOM    756  N   ALA A 238       6.827  -9.045  33.337  1.00 19.06      A
ATOM    757  CA  ALA A 238       7.804  -8.627  32.331  1.00 18.56      A
ATOM    758  CB  ALA A 238       7.097  -7.926  31.173  1.00 19.27      A
ATOM    759  C   ALA A 238       8.887  -7.709  32.913  1.00 18.35      A
```

```
ATOM    760  O   ALA A 238      10.042  -7.760  32.487  1.00 16.90      A
ATOM    761  N   SER A 239       8.514  -6.875  33.885  1.00 17.63      A
ATOM    762  CA  SER A 239       9.465  -5.954  34.514  1.00 16.36      A
ATOM    763  CB  SER A 239       8.742  -4.711  35.040  1.00 16.10      A
ATOM    764  OG  SER A 239       8.150  -3.987  33.978  1.00 13.99      A
ATOM    765  C   SER A 239      10.257  -6.594  35.654  1.00 16.21      A
ATOM    766  O   SER A 239      11.139  -5.960  36.233  1.00 14.92      A
ATOM    767  N   GLY A 240       9.939  -7.847  35.971  1.00 17.34      A
ATOM    768  CA  GLY A 240      10.641  -8.549  37.034  1.00 19.06      A
ATOM    769  C   GLY A 240       9.887  -8.734  38.343  1.00 19.17      A
ATOM    770  O   GLY A 240      10.481  -9.135  39.349  1.00 18.10      A
ATOM    771  N   GLY A 241       8.587  -8.447  38.336  1.00 19.87      A
ATOM    772  CA  GLY A 241       7.785  -8.589  39.544  1.00 21.03      A
ATOM    773  C   GLY A 241       7.571 -10.037  39.955  1.00 23.23      A
ATOM    774  O   GLY A 241       7.305 -10.891  39.101  1.00 20.87      A
ATOM    775  N   ARG A 242       7.683 -10.313  41.258  1.00 23.63      A
ATOM    776  CA  ARG A 242       7.516 -11.667  41.781  1.00 25.27      A
ATOM    777  CB  ARG A 242       8.598 -11.984  42.824  1.00 25.03      A
ATOM    778  CG  ARG A 242      10.024 -11.754  42.341  1.00 24.85      A
ATOM    779  CD  ARG A 242      10.718 -10.684  43.178  1.00 26.43      A
ATOM    780  NE  ARG A 242      11.165 -11.200  44.466  1.00 27.59      A
ATOM    781  CZ  ARG A 242      11.636 -10.450  45.457  1.00 28.68      A
ATOM    782  NH1 ARG A 242      11.724  -9.134  45.325  1.00 28.64      A
ATOM    783  NH2 ARG A 242      12.028 -11.021  46.583  1.00 30.13      A
ATOM    784  C   ARG A 242       6.132 -11.897  42.387  1.00 26.63      A
ATOM    785  O   ARG A 242       5.470 -10.967  42.853  1.00 25.37      A
ATOM    786  N   ARG A 243       5.720 -13.160  42.383  1.00 28.15      A
ATOM    787  CA  ARG A 243       4.415 -13.586  42.881  1.00 31.23      A
ATOM    788  CB  ARG A 243       4.268 -15.095  42.676  1.00 32.92      A
ATOM    789  CG  ARG A 243       5.308 -15.917  43.430  1.00 36.39      A
ATOM    790  CD  ARG A 243       4.923 -17.386  43.486  1.00 38.87      A
ATOM    791  NE  ARG A 243       4.656 -17.908  42.151  1.00 42.37      A
ATOM    792  CZ  ARG A 243       5.564 -17.979  41.183  1.00 43.39      A
ATOM    793  NH1 ARG A 243       6.807 -17.568  41.399  1.00 43.57      A
ATOM    794  NH2 ARG A 243       5.226 -18.454  39.995  1.00 44.19      A
ATOM    795  C   ARG A 243       4.083 -13.271  44.337  1.00 31.11      A
ATOM    796  O   ARG A 243       3.090 -12.608  44.634  1.00 31.87      A
ATOM    797  N   SER A 244       4.915 -13.768  45.240  1.00 32.34      A
ATOM    798  CA  SER A 244       4.706 -13.605  46.671  1.00 33.36      A
ATOM    799  CB  SER A 244       5.399 -14.751  47.400  1.00 34.95      A
ATOM    800  OG  SER A 244       6.798 -14.710  47.156  1.00 37.15      A
ATOM    801  C   SER A 244       5.173 -12.290  47.286  1.00 32.42      A
ATOM    802  O   SER A 244       4.932 -12.045  48.472  1.00 34.13      A
ATOM    803  N   ALA A 245       5.830 -11.449  46.495  1.00 30.06      A
ATOM    804  CA  ALA A 245       6.360 -10.184  46.995  1.00 27.25      A
ATOM    805  CB  ALA A 245       7.360  -9.617  45.989  1.00 26.52      A
ATOM    806  C   ALA A 245       5.334  -9.111  47.359  1.00 25.79      A
ATOM    807  O   ALA A 245       4.293  -8.978  46.720  1.00 26.17      A
ATOM    808  N   THR A 246       5.650  -8.351  48.404  1.00 24.39      A
ATOM    809  CA  THR A 246       4.809  -7.252  48.863  1.00 22.15      A
ATOM    810  CB  THR A 246       5.113  -6.891  50.335  1.00 22.79      A
ATOM    811  OG1 THR A 246       4.507  -7.857  51.196  1.00 20.97      A
ATOM    812  CG2 THR A 246       4.590  -5.500  50.680  1.00 23.06      A
ATOM    813  C   THR A 246       5.160  -6.068  47.968  1.00 22.02      A
ATOM    814  O   THR A 246       6.339  -5.789  47.733  1.00 21.73      A
ATOM    815  N   LYS A 247       4.140  -5.381  47.466  1.00 20.19      A
```

ATOM	816	CA	LYS	A	247	4.345	-4.246	46.574	1.00	19.02	A
ATOM	817	CB	LYS	A	247	3.193	-4.161	45.573	1.00	19.65	A
ATOM	818	CG	LYS	A	247	3.074	-5.343	44.614	1.00	21.06	A
ATOM	819	CD	LYS	A	247	1.889	-5.127	43.680	1.00	23.15	A
ATOM	820	CE	LYS	A	247	1.777	-6.205	42.612	1.00	24.77	A
ATOM	821	NZ	LYS	A	247	0.745	-5.834	41.592	1.00	25.30	A
ATOM	822	C	LYS	A	247	4.477	-2.906	47.296	1.00	17.94	A
ATOM	823	O	LYS	A	247	3.604	-2.517	48.074	1.00	16.18	A
ATOM	824	N	VAL	A	248	5.569	-2.200	47.015	1.00	15.60	A
ATOM	825	CA	VAL	A	248	5.823	-0.895	47.611	1.00	14.60	A
ATOM	826	CB	VAL	A	248	7.005	-0.934	48.606	1.00	12.63	A
ATOM	827	CG1	VAL	A	248	7.176	0.427	49.239	1.00	12.28	A
ATOM	828	CG2	VAL	A	248	6.775	-2.000	49.686	1.00	14.36	A
ATOM	829	C	VAL	A	248	6.179	0.128	46.525	1.00	13.82	A
ATOM	830	O	VAL	A	248	6.907	-0.190	45.581	1.00	14.75	A
ATOM	831	N	MET	A	249	5.664	1.348	46.665	1.00	13.36	A
ATOM	832	CA	MET	A	249	5.958	2.432	45.721	1.00	12.42	A
ATOM	833	CB	MET	A	249	4.715	2.834	44.922	1.00	12.10	A
ATOM	834	CG	MET	A	249	5.019	3.890	43.854	1.00	12.46	A
ATOM	835	SD	MET	A	249	3.586	4.612	43.039	1.00	16.07	A
ATOM	836	CE	MET	A	249	3.108	3.259	41.935	1.00	17.64	A
ATOM	837	C	MET	A	249	6.451	3.636	46.518	1.00	12.45	A
ATOM	838	O	MET	A	249	5.857	3.991	47.538	1.00	13.01	A
ATOM	839	N	VAL	A	250	7.539	4.252	46.060	1.00	11.98	A
ATOM	840	CA	VAL	A	250	8.115	5.412	46.738	1.00	10.91	A
ATOM	841	CB	VAL	A	250	9.590	5.139	47.159	1.00	11.37	A
ATOM	842	CG1	VAL	A	250	10.140	6.308	47.953	1.00	10.05	A
ATOM	843	CG2	VAL	A	250	9.670	3.869	47.978	1.00	9.66	A
ATOM	844	C	VAL	A	250	8.075	6.626	45.805	1.00	10.65	A
ATOM	845	O	VAL	A	250	8.809	6.692	44.814	1.00	9.79	A
ATOM	846	N	VAL	A	251	7.217	7.587	46.128	1.00	8.23	A
ATOM	847	CA	VAL	A	251	7.069	8.776	45.303	1.00	8.84	A
ATOM	848	CB	VAL	A	251	5.578	9.163	45.195	1.00	7.93	A
ATOM	849	CG1	VAL	A	251	5.393	10.275	44.192	1.00	8.30	A
ATOM	850	CG2	VAL	A	251	4.768	7.950	44.791	1.00	6.06	A
ATOM	851	C	VAL	A	251	7.870	9.954	45.846	1.00	7.73	A
ATOM	852	O	VAL	A	251	7.661	10.400	46.974	1.00	8.35	A
ATOM	853	N	VAL	A	252	8.798	10.447	45.040	1.00	7.77	A
ATOM	854	CA	VAL	A	252	9.636	11.572	45.435	1.00	7.58	A
ATOM	855	CB	VAL	A	252	11.122	11.249	45.185	1.00	8.48	A
ATOM	856	CG1	VAL	A	252	12.009	12.339	45.785	1.00	8.93	A
ATOM	857	CG2	VAL	A	252	11.459	9.880	45.769	1.00	8.20	A
ATOM	858	C	VAL	A	252	9.219	12.782	44.599	1.00	7.83	A
ATOM	859	O	VAL	A	252	9.455	12.822	43.382	1.00	8.22	A
ATOM	860	N	THR	A	253	8.602	13.767	45.247	1.00	7.14	A
ATOM	861	CA	THR	A	253	8.124	14.956	44.538	1.00	6.30	A
ATOM	862	CB	THR	A	253	6.795	14.639	43.808	1.00	4.22	A
ATOM	863	OG1	THR	A	253	6.307	15.819	43.163	1.00	6.07	A
ATOM	864	CG2	THR	A	253	5.751	14.116	44.796	1.00	5.03	A
ATOM	865	C	THR	A	253	7.907	16.163	45.449	1.00	6.67	A
ATOM	866	O	THR	A	253	7.897	16.037	46.667	1.00	8.59	A
ATOM	867	N	ASP	A	254	7.726	17.336	44.852	1.00	8.22	A
ATOM	868	CA	ASP	A	254	7.501	18.559	45.618	1.00	7.68	A
ATOM	869	CB	ASP	A	254	8.158	19.756	44.914	1.00	6.78	A
ATOM	870	CG	ASP	A	254	7.714	19.897	43.464	1.00	9.84	A
ATOM	871	OD1	ASP	A	254	6.727	19.230	43.081	1.00	8.18	A

ATOM	872	OD2	ASP	A	254	8.340	20.680	42.714	1.00	9.72	A
ATOM	873	C	ASP	A	254	5.998	18.811	45.796	1.00	7.73	A
ATOM	874	O	ASP	A	254	5.589	19.837	46.339	1.00	6.75	A
ATOM	875	N	GLY	A	255	5.188	17.874	45.314	1.00	7.48	A
ATOM	876	CA	GLY	A	255	3.745	17.981	45.441	1.00	8.81	A
ATOM	877	C	GLY	A	255	3.033	18.954	44.517	1.00	10.43	A
ATOM	878	O	GLY	A	255	1.849	19.212	44.697	1.00	11.40	A
ATOM	879	N	GLU	A	256	3.734	19.480	43.521	1.00	10.74	A
ATOM	880	CA	GLU	A	256	3.141	20.438	42.590	1.00	10.42	A
ATOM	881	CB	GLU	A	256	4.080	21.634	42.434	1.00	10.18	A
ATOM	882	CG	GLU	A	256	3.510	22.804	41.657	1.00	10.67	A
ATOM	883	CD	GLU	A	256	4.526	23.916	41.501	1.00	12.63	A
ATOM	884	OE1	GLU	A	256	5.582	23.679	40.871	1.00	11.76	A
ATOM	885	OE2	GLU	A	256	4.275	25.024	42.018	1.00	17.05	A
ATOM	886	C	GLU	A	256	2.873	19.802	41.224	1.00	11.06	A
ATOM	887	O	GLU	A	256	3.612	20.028	40.267	1.00	9.35	A
ATOM	888	N	SER	A	257	1.800	19.019	41.142	1.00	11.83	A
ATOM	889	CA	SER	A	257	1.429	18.336	39.908	1.00	12.36	A
ATOM	890	CB	SER	A	257	0.797	16.983	40.238	1.00	13.41	A
ATOM	891	OG	SER	A	257	-0.402	17.165	40.973	1.00	15.55	A
ATOM	892	C	SER	A	257	0.449	19.130	39.055	1.00	12.39	A
ATOM	893	O	SER	A	257	-0.123	20.119	39.500	1.00	11.98	A
ATOM	894	N	HIS	A	258	0.259	18.678	37.819	1.00	13.45	A
ATOM	895	CA	HIS	A	258	-0.676	19.313	36.904	1.00	13.92	A
ATOM	896	CB	HIS	A	258	-0.047	19.496	35.514	1.00	14.39	A
ATOM	897	CG	HIS	A	258	0.973	20.588	35.446	1.00	15.31	A
ATOM	898	CD2	HIS	A	258	0.856	21.893	35.100	1.00	16.93	A
ATOM	899	ND1	HIS	A	258	2.297	20.399	35.783	1.00	15.95	A
ATOM	900	CE1	HIS	A	258	2.949	21.540	35.648	1.00	17.37	A
ATOM	901	NE2	HIS	A	258	2.099	22.463	35.236	1.00	15.99	A
ATOM	902	C	HIS	A	258	-1.928	18.444	36.781	1.00	14.43	A
ATOM	903	O	HIS	A	258	-3.002	18.940	36.428	1.00	14.21	A
ATOM	904	N	ASP	A	259	-1.788	17.152	37.081	1.00	13.61	A
ATOM	905	CA	ASP	A	259	-2.916	16.228	36.972	1.00	14.20	A
ATOM	906	CB	ASP	A	259	-2.536	15.034	36.076	1.00	14.11	A
ATOM	907	CG	ASP	A	259	-1.374	14.212	36.632	1.00	14.29	A
ATOM	908	OD1	ASP	A	259	-0.966	14.438	37.791	1.00	12.82	A
ATOM	909	OD2	ASP	A	259	-0.878	13.323	35.905	1.00	12.48	A
ATOM	910	C	ASP	A	259	-3.499	15.713	38.296	1.00	14.24	A
ATOM	911	O	ASP	A	259	-3.927	14.557	38.384	1.00	13.26	A
ATOM	912	N	GLY	A	260	-3.531	16.575	39.309	1.00	13.52	A
ATOM	913	CA	GLY	A	260	-4.072	16.190	40.601	1.00	15.49	A
ATOM	914	C	GLY	A	260	-5.550	15.814	40.601	1.00	17.20	A
ATOM	915	O	GLY	A	260	-6.059	15.265	41.584	1.00	17.99	A
ATOM	916	N	SER	A	261	-6.255	16.100	39.515	1.00	17.56	A
ATOM	917	CA	SER	A	261	-7.672	15.764	39.453	1.00	20.43	A
ATOM	918	CB	SER	A	261	-8.303	16.341	38.183	1.00	19.97	A
ATOM	919	OG	SER	A	261	-7.769	15.726	37.025	1.00	22.72	A
ATOM	920	C	SER	A	261	-7.880	14.246	39.485	1.00	21.99	A
ATOM	921	O	SER	A	261	-8.981	13.769	39.766	1.00	23.07	A
ATOM	922	N	MET	A	262	-6.817	13.494	39.211	1.00	22.29	A
ATOM	923	CA	MET	A	262	-6.880	12.038	39.193	1.00	22.48	A
ATOM	924	CB	MET	A	262	-5.974	11.494	38.087	1.00	23.03	A
ATOM	925	CG	MET	A	262	-6.258	12.065	36.708	1.00	24.64	A
ATOM	926	SD	MET	A	262	-5.131	11.417	35.452	1.00	27.40	A
ATOM	927	CE	MET	A	262	-3.565	11.957	36.091	1.00	27.77	A

ATOM	928	C	MET	A	262	-6.492	11.387	40.523	1.00 22.57	A
ATOM	929	O	MET	A	262	-6.538	10.168	40.655	1.00 23.23	A
ATOM	930	N	LEU	A	263	-6.107	12.197	41.502	1.00 23.04	A
ATOM	931	CA	LEU	A	263	-5.707	11.694	42.817	1.00 23.03	A
ATOM	932	CB	LEU	A	263	-5.775	12.839	43.840	1.00 22.96	A
ATOM	933	CG	LEU	A	263	-5.290	12.652	45.285	1.00 22.74	A
ATOM	934	CD1	LEU	A	263	-5.364	13.999	45.984	1.00 24.94	A
ATOM	935	CD2	LEU	A	263	-6.134	11.637	46.038	1.00 23.03	A
ATOM	936	C	LEU	A	263	-6.552	10.511	43.310	1.00 22.95	A
ATOM	937	O	LEU	A	263	-6.071	9.376	43.398	1.00 23.38	A
ATOM	938	N	LYS	A	264	-7.807	10.799	43.642	1.00 22.68	A
ATOM	939	CA	LYS	A	264	-8.761	9.811	44.154	1.00 22.38	A
ATOM	940	CB	LYS	A	264	-10.162	10.429	44.161	1.00 22.83	A
ATOM	941	CG	LYS	A	264	-11.251	9.581	44.782	1.00 23.74	A
ATOM	942	CD	LYS	A	264	-11.152	9.568	46.291	1.00 25.46	A
ATOM	943	CE	LYS	A	264	-12.536	9.481	46.904	1.00 27.18	A
ATOM	944	NZ	LYS	A	264	-13.317	8.347	46.335	1.00 27.63	A
ATOM	945	C	LYS	A	264	-8.793	8.513	43.352	1.00 21.28	A
ATOM	946	O	LYS	A	264	-8.706	7.417	43.913	1.00 19.95	A
ATOM	947	N	ALA	A	265	-8.925	8.651	42.037	1.00 20.39	A
ATOM	948	CA	ALA	A	265	-8.991	7.508	41.136	1.00 18.47	A
ATOM	949	CB	ALA	A	265	-9.264	7.989	39.715	1.00 19.33	A
ATOM	950	C	ALA	A	265	-7.742	6.637	41.153	1.00 17.32	A
ATOM	951	O	ALA	A	265	-7.838	5.412	41.229	1.00 16.33	A
ATOM	952	N	VAL	A	266	-6.573	7.267	41.079	1.00 15.33	A
ATOM	953	CA	VAL	A	266	-5.312	6.530	41.063	1.00 14.14	A
ATOM	954	CB	VAL	A	266	-4.163	7.449	40.580	1.00 15.25	A
ATOM	955	CG1	VAL	A	266	-2.822	6.744	40.713	1.00 12.74	A
ATOM	956	CG2	VAL	A	266	-4.412	7.845	39.122	1.00 14.35	A
ATOM	957	C	VAL	A	266	-4.953	5.907	42.417	1.00 13.82	A
ATOM	958	O	VAL	A	266	-4.544	4.744	42.493	1.00 11.03	A
ATOM	959	N	ILE	A	267	-5.123	6.679	43.483	1.00 13.92	A
ATOM	960	CA	ILE	A	267	-4.820	6.203	44.826	1.00 14.29	A
ATOM	961	CB	ILE	A	267	-4.981	7.353	45.849	1.00 13.44	A
ATOM	962	CG2	ILE	A	267	-4.768	6.845	47.269	1.00 12.64	A
ATOM	963	CG1	ILE	A	267	-3.994	8.475	45.503	1.00 13.65	A
ATOM	964	CD1	ILE	A	267	-2.565	8.013	45.313	1.00 12.83	A
ATOM	965	C	ILE	A	267	-5.708	5.019	45.220	1.00 15.77	A
ATOM	966	O	ILE	A	267	-5.248	4.081	45.869	1.00 14.63	A
ATOM	967	N	ASP	A	268	-6.976	5.064	44.820	1.00 17.07	A
ATOM	968	CA	ASP	A	268	-7.908	3.985	45.133	1.00 18.52	A
ATOM	969	CB	ASP	A	268	-9.293	4.292	44.567	1.00 21.82	A
ATOM	970	CG	ASP	A	268	-10.330	4.518	45.646	1.00 24.24	A
ATOM	971	OD1	ASP	A	268	-10.429	3.674	46.566	1.00 27.22	A
ATOM	972	OD2	ASP	A	268	-11.055	5.532	45.566	1.00 25.15	A
ATOM	973	C	ASP	A	268	-7.408	2.681	44.530	1.00 18.70	A
ATOM	974	O	ASP	A	268	-7.378	1.642	45.195	1.00 17.59	A
ATOM	975	N	GLN	A	269	-7.017	2.742	43.260	1.00 17.82	A
ATOM	976	CA	GLN	A	269	-6.520	1.559	42.571	1.00 17.98	A
ATOM	977	CB	GLN	A	269	-6.177	1.894	41.121	1.00 19.75	A
ATOM	978	CG	GLN	A	269	-7.371	2.329	40.299	1.00 24.17	A
ATOM	979	CD	GLN	A	269	-7.025	2.532	38.839	1.00 27.38	A
ATOM	980	OE1	GLN	A	269	-6.679	1.583	38.133	1.00 31.17	A
ATOM	981	NE2	GLN	A	269	-7.112	3.773	38.377	1.00 28.54	A
ATOM	982	C	GLN	A	269	-5.295	1.005	43.282	1.00 16.45	A
ATOM	983	O	GLN	A	269	-5.183	-0.207	43.487	1.00 13.95	A

ATOM	984	N	CYS	A	270	-4.378	1.896	43.657	1.00	14.73	A
ATOM	985	CA	CYS	A	270	-3.175	1.478	44.359	1.00	15.16	A
ATOM	986	CB	CYS	A	270	-2.299	2.688	44.709	1.00	14.54	A
ATOM	987	SG	CYS	A	270	-1.455	3.488	43.295	1.00	12.41	A
ATOM	988	C	CYS	A	270	-3.570	0.730	45.627	1.00	15.14	A
ATOM	989	O	CYS	A	270	-2.974	-0.294	45.957	1.00	15.57	A
ATOM	990	N	ASN	A	271	-4.587	1.228	46.329	1.00	17.79	A
ATOM	991	CA	ASN	A	271	-5.042	0.577	47.556	1.00	18.54	A
ATOM	992	CB	ASN	A	271	-6.154	1.383	48.240	1.00	18.69	A
ATOM	993	CG	ASN	A	271	-5.628	2.595	48.997	1.00	19.21	A
ATOM	994	OD1	ASN	A	271	-4.474	2.628	49.423	1.00	19.65	A
ATOM	995	ND2	ASN	A	271	-6.485	3.586	49.188	1.00	18.35	A
ATOM	996	C	ASN	A	271	-5.534	-0.843	47.297	1.00	19.85	A
ATOM	997	O	ASN	A	271	-5.217	-1.756	48.054	1.00	19.38	A
ATOM	998	N	HIS	A	272	-6.298	-1.034	46.225	1.00	20.77	A
ATOM	999	CA	HIS	A	272	-6.816	-2.361	45.898	1.00	22.45	A
ATOM	1000	CB	HIS	A	272	-7.961	-2.240	44.894	1.00	26.64	A
ATOM	1001	CG	HIS	A	272	-9.210	-1.673	45.494	1.00	30.29	A
ATOM	1002	CD2	HIS	A	272	-9.798	-0.464	45.353	1.00	31.55	A
ATOM	1003	ND1	HIS	A	272	-9.955	-2.355	46.432	1.00	32.65	A
ATOM	1004	CE1	HIS	A	272	-10.947	-1.588	46.847	1.00	32.98	A
ATOM	1005	NE2	HIS	A	272	-10.874	-0.433	46.208	1.00	33.31	A
ATOM	1006	C	HIS	A	272	-5.756	-3.337	45.398	1.00	21.74	A
ATOM	1007	O	HIS	A	272	-5.947	-4.549	45.475	1.00	21.48	A
ATOM	1008	N	ASP	A	273	-4.644	-2.811	44.883	1.00	20.99	A
ATOM	1009	CA	ASP	A	273	-3.536	-3.650	44.420	1.00	19.25	A
ATOM	1010	CB	ASP	A	273	-2.721	-2.943	43.330	1.00	18.34	A
ATOM	1011	CG	ASP	A	273	-3.410	-2.952	41.979	1.00	18.54	A
ATOM	1012	OD1	ASP	A	273	-4.474	-3.584	41.851	1.00	18.73	A
ATOM	1013	OD2	ASP	A	273	-2.883	-2.326	41.039	1.00	19.50	A
ATOM	1014	C	ASP	A	273	-2.628	-3.923	45.617	1.00	18.38	A
ATOM	1015	O	ASP	A	273	-1.597	-4.586	45.497	1.00	17.39	A
ATOM	1016	N	ASN	A	274	-3.025	-3.395	46.771	1.00	18.11	A
ATOM	1017	CA	ASN	A	274	-2.276	-3.552	48.013	1.00	17.29	A
ATOM	1018	CB	ASN	A	274	-2.258	-5.016	48.450	1.00	18.34	A
ATOM	1019	CG	ASN	A	274	-3.650	-5.565	48.681	1.00	20.60	A
ATOM	1020	OD1	ASN	A	274	-4.483	-4.927	49.331	1.00	20.94	A
ATOM	1021	ND2	ASN	A	274	-3.912	-6.754	48.154	1.00	22.78	A
ATOM	1022	C	ASN	A	274	-0.855	-3.037	47.889	1.00	16.90	A
ATOM	1023	O	ASN	A	274	0.104	-3.725	48.249	1.00	16.67	A
ATOM	1024	N	ILE	A	275	-0.725	-1.819	47.375	1.00	16.97	A
ATOM	1025	CA	ILE	A	275	0.583	-1.194	47.210	1.00	15.59	A
ATOM	1026	CB	ILE	A	275	0.693	-0.453	45.855	1.00	14.51	A
ATOM	1027	CG2	ILE	A	275	2.027	0.279	45.764	1.00	13.97	A
ATOM	1028	CG1	ILE	A	275	0.563	-1.442	44.699	1.00	14.72	A
ATOM	1029	CD1	ILE	A	275	0.834	-0.824	43.342	1.00	13.73	A
ATOM	1030	C	ILE	A	275	0.829	-0.189	48.335	1.00	15.36	A
ATOM	1031	O	ILE	A	275	0.092	0.789	48.475	1.00	14.71	A
ATOM	1032	N	LEU	A	276	1.856	-0.446	49.143	1.00	15.48	A
ATOM	1033	CA	LEU	A	276	2.217	0.448	50.240	1.00	15.30	A
ATOM	1034	CB	LEU	A	276	3.178	-0.248	51.204	1.00	17.87	A
ATOM	1035	CG	LEU	A	276	2.627	-1.353	52.108	1.00	20.34	A
ATOM	1036	CD1	LEU	A	276	1.537	-0.773	52.994	1.00	22.51	A
ATOM	1037	CD2	LEU	A	276	2.091	-2.504	51.268	1.00	21.16	A
ATOM	1038	C	LEU	A	276	2.906	1.652	49.619	1.00	14.60	A
ATOM	1039	O	LEU	A	276	3.788	1.482	48.777	1.00	16.04	A

ATOM	1040	N	ARG	A	277	2.524	2.859	50.036	1.00	13.49	A
ATOM	1041	CA	ARG	A	277	3.101	4.074	49.463	1.00	12.06	A
ATOM	1042	CB	ARG	A	277	2.026	4.855	48.698	1.00	10.92	A
ATOM	1043	CG	ARG	A	277	1.334	4.078	47.586	1.00	6.86	A
ATOM	1044	CD	ARG	A	277	0.192	4.898	46.985	1.00	6.96	A
ATOM	1045	NE	ARG	A	277	-0.789	5.303	47.992	1.00	6.18	A
ATOM	1046	CZ	ARG	A	277	-1.687	4.492	48.543	1.00	7.31	A
ATOM	1047	NH1	ARG	A	277	-2.537	4.955	49.452	1.00	6.68	A
ATOM	1048	NH2	ARG	A	277	-1.748	3.217	48.182	1.00	7.09	A
ATOM	1049	C	ARG	A	277	3.788	5.050	50.414	1.00	11.97	A
ATOM	1050	O	ARG	A	277	3.225	5.453	51.431	1.00	13.23	A
ATOM	1051	N	PHE	A	278	5.009	5.435	50.057	1.00	10.69	A
ATOM	1052	CA	PHE	A	278	5.767	6.409	50.826	1.00	11.20	A
ATOM	1053	CB	PHE	A	278	7.239	6.000	50.983	1.00	9.58	A
ATOM	1054	CG	PHE	A	278	7.484	4.944	52.027	1.00	11.91	A
ATOM	1055	CD1	PHE	A	278	7.231	3.603	51.759	1.00	12.77	A
ATOM	1056	CD2	PHE	A	278	7.985	5.293	53.280	1.00	12.69	A
ATOM	1057	CE1	PHE	A	278	7.475	2.620	52.727	1.00	12.09	A
ATOM	1058	CE2	PHE	A	278	8.230	4.318	54.251	1.00	13.27	A
ATOM	1059	CZ	PHE	A	278	7.974	2.978	53.969	1.00	11.23	A
ATOM	1060	C	PHE	A	278	5.718	7.717	50.042	1.00	11.02	A
ATOM	1061	O	PHE	A	278	5.787	7.718	48.808	1.00	12.54	A
ATOM	1062	N	GLY	A	279	5.587	8.822	50.758	1.00	10.43	A
ATOM	1063	CA	GLY	A	279	5.579	10.121	50.114	1.00	10.44	A
ATOM	1064	C	GLY	A	279	6.841	10.824	50.572	1.00	10.00	A
ATOM	1065	O	GLY	A	279	7.000	11.069	51.767	1.00	8.22	A
ATOM	1066	N	ILE	A	280	7.741	11.135	49.641	1.00	9.32	A
ATOM	1067	CA	ILE	A	280	9.006	11.800	49.976	1.00	8.94	A
ATOM	1068	CB	ILE	A	280	10.210	11.086	49.297	1.00	9.74	A
ATOM	1069	CG2	ILE	A	280	11.518	11.635	49.851	1.00	6.76	A
ATOM	1070	CG1	ILE	A	280	10.104	9.564	49.484	1.00	7.75	A
ATOM	1071	CD1	ILE	A	280	10.002	9.104	50.927	1.00	8.44	A
ATOM	1072	C	ILE	A	280	8.982	13.258	49.511	1.00	9.08	A
ATOM	1073	O	ILE	A	280	9.072	13.540	48.314	1.00	8.74	A
ATOM	1074	N	ALA	A	281	8.890	14.183	50.461	1.00	8.56	A
ATOM	1075	CA	ALA	A	281	8.813	15.606	50.132	1.00	9.58	A
ATOM	1076	CB	ALA	A	281	8.092	16.351	51.255	1.00	9.06	A
ATOM	1077	C	ALA	A	281	10.112	16.335	49.793	1.00	9.24	A
ATOM	1078	O	ALA	A	281	10.994	16.500	50.631	1.00	9.20	A
ATOM	1079	N	VAL	A	282	10.202	16.773	48.544	1.00	9.69	A
ATOM	1080	CA	VAL	A	282	11.334	17.544	48.058	1.00	11.46	A
ATOM	1081	CB	VAL	A	282	11.549	17.337	46.539	1.00	12.19	A
ATOM	1082	CG1	VAL	A	282	12.695	18.198	46.046	1.00	10.75	A
ATOM	1083	CG2	VAL	A	282	11.823	15.861	46.245	1.00	12.21	A
ATOM	1084	C	VAL	A	282	10.899	18.986	48.306	1.00	12.35	A
ATOM	1085	O	VAL	A	282	10.298	19.629	47.444	1.00	12.44	A
ATOM	1086	N	LEU	A	283	11.173	19.473	49.509	1.00	12.18	A
ATOM	1087	CA	LEU	A	283	10.808	20.829	49.898	1.00	12.59	A
ATOM	1088	CB	LEU	A	283	9.432	20.839	50.584	1.00	11.98	A
ATOM	1089	CG	LEU	A	283	8.169	20.217	49.972	1.00	11.80	A
ATOM	1090	CD1	LEU	A	283	7.058	20.286	51.002	1.00	10.46	A
ATOM	1091	CD2	LEU	A	283	7.747	20.940	48.698	1.00	11.27	A
ATOM	1092	C	LEU	A	283	11.852	21.323	50.892	1.00	13.20	A
ATOM	1093	O	LEU	A	283	12.496	20.515	51.565	1.00	13.05	A
ATOM	1094	N	GLY	A	284	12.028	22.641	50.977	1.00	15.10	A
ATOM	1095	CA	GLY	A	284	12.973	23.191	51.931	1.00	16.65	A

ATOM	1096	C	GLY	A	284	14.057	24.118	51.408	1.00	18.34	A
ATOM	1097	O	GLY	A	284	14.597	24.927	52.163	1.00	17.39	A
ATOM	1098	N	TYR	A	285	14.379	24.007	50.126	1.00	19.40	A
ATOM	1099	CA	TYR	A	285	15.424	24.829	49.528	1.00	21.96	A
ATOM	1100	CB	TYR	A	285	16.262	23.973	48.591	1.00	22.25	A
ATOM	1101	CG	TYR	A	285	16.946	22.812	49.285	1.00	25.63	A
ATOM	1102	CD1	TYR	A	285	18.230	22.950	49.816	1.00	25.35	A
ATOM	1103	CE1	TYR	A	285	18.878	21.869	50.420	1.00	27.84	A
ATOM	1104	CD2	TYR	A	285	16.321	21.564	49.383	1.00	24.77	A
ATOM	1105	CE2	TYR	A	285	16.958	20.483	49.983	1.00	25.71	A
ATOM	1106	CZ	TYR	A	285	18.236	20.639	50.498	1.00	27.19	A
ATOM	1107	OH	TYR	A	285	18.880	19.567	51.081	1.00	28.61	A
ATOM	1108	C	TYR	A	285	14.863	26.032	48.781	1.00	22.57	A
ATOM	1109	O	TYR	A	285	15.523	27.062	48.669	1.00	24.02	A
ATOM	1110	N	LEU	A	286	13.645	25.896	48.268	1.00	23.97	A
ATOM	1111	CA	LEU	A	286	12.991	26.984	47.553	1.00	24.44	A
ATOM	1112	CB	LEU	A	286	12.109	26.433	46.424	1.00	23.78	A
ATOM	1113	CG	LEU	A	286	12.733	25.452	45.424	1.00	23.33	A
ATOM	1114	CD1	LEU	A	286	11.768	25.238	44.268	1.00	22.08	A
ATOM	1115	CD2	LEU	A	286	14.052	25.995	44.895	1.00	23.54	A
ATOM	1116	C	LEU	A	286	12.130	27.754	48.550	1.00	25.62	A
ATOM	1117	O	LEU	A	286	11.432	27.158	49.367	1.00	25.02	A
ATOM	1118	N	ASN	A	287	12.185	29.079	48.484	1.00	28.24	A
ATOM	1119	CA	ASN	A	287	11.414	29.924	49.391	1.00	28.80	A
ATOM	1120	CB	ASN	A	287	12.072	31.298	49.505	1.00	30.42	A
ATOM	1121	CG	ASN	A	287	11.674	32.030	50.769	1.00	31.82	A
ATOM	1122	OD1	ASN	A	287	10.490	32.180	51.072	1.00	32.26	A
ATOM	1123	ND2	ASN	A	287	12.667	32.496	51.513	1.00	33.25	A
ATOM	1124	C	ASN	A	287	9.980	30.085	48.901	1.00	29.54	A
ATOM	1125	O	ASN	A	287	9.740	30.651	47.833	1.00	29.75	A
ATOM	1126	N	ARG	A	288	9.029	29.594	49.688	1.00	29.81	A
ATOM	1127	CA	ARG	A	288	7.614	29.677	49.331	1.00	30.68	A
ATOM	1128	CB	ARG	A	288	7.063	28.285	49.002	1.00	30.29	A
ATOM	1129	CG	ARG	A	288	7.722	27.568	47.834	1.00	27.73	A
ATOM	1130	CD	ARG	A	288	6.856	26.381	47.427	1.00	28.24	A
ATOM	1131	NE	ARG	A	288	7.279	25.765	46.173	1.00	26.45	A
ATOM	1132	CZ	ARG	A	288	8.232	24.846	46.075	1.00	27.37	A
ATOM	1133	NH1	ARG	A	288	8.866	24.430	47.164	1.00	26.30	A
ATOM	1134	NH2	ARG	A	288	8.550	24.342	44.888	1.00	26.61	A
ATOM	1135	C	ARG	A	288	6.798	30.267	50.477	1.00	31.67	A
ATOM	1136	O	ARG	A	288	7.298	30.396	51.591	1.00	31.76	A
ATOM	1137	N	ASN	A	289	5.544	30.621	50.196	1.00	33.77	A
ATOM	1138	CA	ASN	A	289	4.646	31.176	51.212	1.00	35.84	A
ATOM	1139	CB	ASN	A	289	3.265	31.491	50.624	1.00	36.52	A
ATOM	1140	CG	ASN	A	289	3.293	32.598	49.611	1.00	37.86	A
ATOM	1141	OD1	ASN	A	289	3.777	33.697	49.883	1.00	39.91	A
ATOM	1142	ND2	ASN	A	289	2.753	32.325	48.431	1.00	38.60	A
ATOM	1143	C	ASN	A	289	4.429	30.146	52.310	1.00	36.64	A
ATOM	1144	O	ASN	A	289	5.315	29.358	52.642	1.00	37.87	A
ATOM	1145	N	ALA	A	290	3.220	30.165	52.861	1.00	36.43	A
ATOM	1146	CA	ALA	A	290	2.815	29.225	53.894	1.00	35.71	A
ATOM	1147	CB	ALA	A	290	2.333	29.970	55.133	1.00	35.62	A
ATOM	1148	C	ALA	A	290	1.673	28.423	53.275	1.00	35.14	A
ATOM	1149	O	ALA	A	290	1.576	27.210	53.458	1.00	34.29	A
ATOM	1150	N	LEU	A	291	0.820	29.120	52.527	1.00	34.35	A
ATOM	1151	CA	LEU	A	291	-0.315	28.498	51.857	1.00	33.93	A

ATOM	1152	CB	LEU	A	291	-1.304	29.563	51.378	1.00	34.50	A
ATOM	1153	CG	LEU	A	291	-2.443	29.050	50.486	1.00	35.78	A
ATOM	1154	CD1	LEU	A	291	-3.223	27.957	51.211	1.00	35.87	A
ATOM	1155	CD2	LEU	A	291	-3.358	30.205	50.108	1.00	35.64	A
ATOM	1156	C	LEU	A	291	0.151	27.672	50.665	1.00	33.30	A
ATOM	1157	O	LEU	A	291	-0.473	26.670	50.309	1.00	33.11	A
ATOM	1158	N	ASP	A	292	1.241	28.109	50.041	1.00	32.39	A
ATOM	1159	CA	ASP	A	292	1.795	27.401	48.898	1.00	30.79	A
ATOM	1160	CB	ASP	A	292	2.782	28.298	48.144	1.00	31.69	A
ATOM	1161	CG	ASP	A	292	2.084	29.335	47.269	1.00	32.74	A
ATOM	1162	OD1	ASP	A	292	2.768	30.243	46.753	1.00	33.80	A
ATOM	1163	OD2	ASP	A	292	0.854	29.237	47.084	1.00	32.42	A
ATOM	1164	C	ASP	A	292	2.493	26.144	49.395	1.00	29.78	A
ATOM	1165	O	ASP	A	292	2.436	25.104	48.754	1.00	29.16	A
ATOM	1166	N	THR	A	293	3.143	26.247	50.548	1.00	29.30	A
ATOM	1167	CA	THR	A	293	3.842	25.109	51.132	1.00	28.64	A
ATOM	1168	CB	THR	A	293	4.788	25.548	52.273	1.00	29.16	A
ATOM	1169	OG1	THR	A	293	5.832	26.379	51.747	1.00	29.06	A
ATOM	1170	CG2	THR	A	293	5.409	24.330	52.942	1.00	29.62	A
ATOM	1171	C	THR	A	293	2.836	24.104	51.691	1.00	28.42	A
ATOM	1172	O	THR	A	293	3.013	22.890	51.556	1.00	28.33	A
ATOM	1173	N	LYS	A	294	1.781	24.614	52.319	1.00	27.12	A
ATOM	1174	CA	LYS	A	294	0.754	23.753	52.894	1.00	25.88	A
ATOM	1175	CB	LYS	A	294	-0.296	24.585	53.631	1.00	27.50	A
ATOM	1176	CG	LYS	A	294	-0.503	24.160	55.074	1.00	31.01	A
ATOM	1177	CD	LYS	A	294	0.711	24.528	55.925	1.00	32.77	A
ATOM	1178	CE	LYS	A	294	0.624	23.964	57.345	1.00	32.54	A
ATOM	1179	NZ	LYS	A	294	1.096	22.554	57.413	1.00	34.00	A
ATOM	1180	C	LYS	A	294	0.070	22.922	51.815	1.00	23.90	A
ATOM	1181	O	LYS	A	294	-0.100	21.713	51.960	1.00	22.61	A
ATOM	1182	N	ASN	A	295	-0.329	23.575	50.732	1.00	21.38	A
ATOM	1183	CA	ASN	A	295	-0.992	22.870	49.646	1.00	21.12	A
ATOM	1184	CB	ASN	A	295	-1.479	23.863	48.594	1.00	23.57	A
ATOM	1185	CG	ASN	A	295	-2.890	24.347	48.870	1.00	26.26	A
ATOM	1186	OD1	ASN	A	295	-3.860	23.616	48.666	1.00	28.01	A
ATOM	1187	ND2	ASN	A	295	-3.010	25.581	49.347	1.00	27.75	A
ATOM	1188	C	ASN	A	295	-0.077	21.825	49.020	1.00	18.46	A
ATOM	1189	O	ASN	A	295	-0.547	20.788	48.554	1.00	16.78	A
ATOM	1190	N	LEU	A	296	1.226	22.098	49.018	1.00	15.33	A
ATOM	1191	CA	LEU	A	296	2.191	21.153	48.469	1.00	14.78	A
ATOM	1192	CB	LEU	A	296	3.571	21.809	48.321	1.00	14.17	A
ATOM	1193	CG	LEU	A	296	3.720	22.917	47.271	1.00	15.83	A
ATOM	1194	CD1	LEU	A	296	5.130	23.495	47.336	1.00	13.92	A
ATOM	1195	CD2	LEU	A	296	3.424	22.359	45.877	1.00	15.72	A
ATOM	1196	C	LEU	A	296	2.288	19.937	49.391	1.00	13.30	A
ATOM	1197	O	LEU	A	296	2.190	18.798	48.939	1.00	13.73	A
ATOM	1198	N	ILE	A	297	2.479	20.184	50.681	1.00	13.90	A
ATOM	1199	CA	ILE	A	297	2.578	19.107	51.664	1.00	12.57	A
ATOM	1200	CB	ILE	A	297	2.704	19.667	53.099	1.00	13.20	A
ATOM	1201	CG2	ILE	A	297	2.581	18.539	54.120	1.00	10.79	A
ATOM	1202	CG1	ILE	A	297	4.041	20.389	53.263	1.00	13.18	A
ATOM	1203	CD1	ILE	A	297	4.169	21.157	54.579	1.00	13.83	A
ATOM	1204	C	ILE	A	297	1.336	18.229	51.601	1.00	13.43	A
ATOM	1205	O	ILE	A	297	1.426	16.999	51.647	1.00	14.67	A
ATOM	1206	N	LYS	A	298	0.173	18.867	51.498	1.00	13.02	A
ATOM	1207	CA	LYS	A	298	-1.089	18.147	51.435	1.00	14.37	A

```
ATOM   1208  CB  LYS A 298      -2.245  19.114  51.175  1.00 15.32      A
ATOM   1209  CG  LYS A 298      -3.565  18.420  50.872  1.00 17.06      A
ATOM   1210  CD  LYS A 298      -4.742  19.363  51.029  1.00 18.40      A
ATOM   1211  CE  LYS A 298      -4.571  20.626  50.198  1.00 19.78      A
ATOM   1212  NZ  LYS A 298      -5.760  21.518  50.326  1.00 20.25      A
ATOM   1213  C   LYS A 298      -1.101  17.054  50.372  1.00 13.87      A
ATOM   1214  O   LYS A 298      -1.484  15.920  50.652  1.00 14.22      A
ATOM   1215  N   GLU A 299      -0.685  17.394  49.155  1.00 14.10      A
ATOM   1216  CA  GLU A 299      -0.666  16.411  48.078  1.00 13.13      A
ATOM   1217  CB  GLU A 299      -0.296  17.056  46.737  1.00 13.37      A
ATOM   1218  CG  GLU A 299      -0.391  16.065  45.571  1.00 14.38      A
ATOM   1219  CD  GLU A 299      -0.037  16.669  44.227  1.00 13.17      A
ATOM   1220  OE1 GLU A 299       1.136  16.562  43.805  1.00 13.60      A
ATOM   1221  OE2 GLU A 299      -0.936  17.257  43.595  1.00 13.39      A
ATOM   1222  C   GLU A 299       0.317  15.289  48.369  1.00 11.75      A
ATOM   1223  O   GLU A 299       0.023  14.121  48.134  1.00 12.23      A
ATOM   1224  N   ILE A 300       1.486  15.636  48.885  1.00 11.21      A
ATOM   1225  CA  ILE A 300       2.480  14.616  49.168  1.00  9.40      A
ATOM   1226  CB  ILE A 300       3.817  15.251  49.613  1.00  9.90      A
ATOM   1227  CG2 ILE A 300       4.856  14.164  49.842  1.00  7.33      A
ATOM   1228  CG1 ILE A 300       4.306  16.222  48.531  1.00  9.03      A
ATOM   1229  CD1 ILE A 300       5.517  17.046  48.922  1.00 10.70      A
ATOM   1230  C   ILE A 300       1.980  13.633  50.222  1.00 10.09      A
ATOM   1231  O   ILE A 300       2.172  12.425  50.084  1.00  9.54      A
ATOM   1232  N   LYS A 301       1.332  14.143  51.268  1.00 10.44      A
ATOM   1233  CA  LYS A 301       0.805  13.280  52.324  1.00 10.83      A
ATOM   1234  CB  LYS A 301       0.377  14.111  53.546  1.00 11.26      A
ATOM   1235  CG  LYS A 301       1.514  14.819  54.281  1.00  9.39      A
ATOM   1236  CD  LYS A 301       1.026  15.364  55.618  1.00  8.55      A
ATOM   1237  CE  LYS A 301       2.156  16.015  56.411  1.00  8.26      A
ATOM   1238  NZ  LYS A 301       1.803  16.140  57.858  1.00  8.59      A
ATOM   1239  C   LYS A 301      -0.393  12.476  51.812  1.00 10.73      A
ATOM   1240  O   LYS A 301      -0.679  11.382  52.300  1.00 10.91      A
ATOM   1241  N   ALA A 302      -1.087  13.033  50.828  1.00  9.99      A
ATOM   1242  CA  ALA A 302      -2.250  12.389  50.232  1.00  9.05      A
ATOM   1243  CB  ALA A 302      -3.002  13.389  49.348  1.00  7.59      A
ATOM   1244  C   ALA A 302      -1.846  11.170  49.414  1.00  8.86      A
ATOM   1245  O   ALA A 302      -2.646  10.265  49.199  1.00  8.67      A
ATOM   1246  N   ILE A 303      -0.600  11.151  48.960  1.00  9.67      A
ATOM   1247  CA  ILE A 303      -0.083  10.041  48.166  1.00 10.19      A
ATOM   1248  CB  ILE A 303       1.121  10.510  47.291  1.00  9.99      A
ATOM   1249  CG2 ILE A 303       1.770   9.326  46.599  1.00  8.69      A
ATOM   1250  CG1 ILE A 303       0.644  11.539  46.258  1.00 11.14      A
ATOM   1251  CD1 ILE A 303       1.781  12.236  45.465  1.00 10.23      A
ATOM   1252  C   ILE A 303       0.357   8.890  49.080  1.00 11.36      A
ATOM   1253  O   ILE A 303       0.172   7.715  48.760  1.00  9.99      A
ATOM   1254  N   ALA A 304       0.935   9.233  50.225  1.00 11.53      A
ATOM   1255  CA  ALA A 304       1.402   8.225  51.162  1.00 11.59      A
ATOM   1256  CB  ALA A 304       2.190   8.885  52.274  1.00 11.10      A
ATOM   1257  C   ALA A 304       0.271   7.391  51.757  1.00 12.66      A
ATOM   1258  O   ALA A 304      -0.883   7.818  51.806  1.00 13.35      A
ATOM   1259  N   SER A 305       0.617   6.189  52.203  1.00 13.47      A
ATOM   1260  CA  SER A 305      -0.348   5.297  52.825  1.00 14.24      A
ATOM   1261  CB  SER A 305       0.188   3.863  52.845  1.00 12.61      A
ATOM   1262  OG  SER A 305       0.197   3.295  51.553  1.00 15.04      A
ATOM   1263  C   SER A 305      -0.598   5.755  54.259  1.00 14.09      A
```

ATOM	1264	O	SER	A	305	0.227	6.451	54.850	1.00	13.19	A
ATOM	1265	N	ILE	A	306	-1.739	5.361	54.814	1.00	14.63	A
ATOM	1266	CA	ILE	A	306	-2.082	5.711	56.189	1.00	15.34	A
ATOM	1267	CB	ILE	A	306	-3.601	5.980	56.316	1.00	16.66	A
ATOM	1268	CG2	ILE	A	306	-3.960	6.292	57.758	1.00	15.49	A
ATOM	1269	CG1	ILE	A	306	-3.997	7.141	55.400	1.00	16.61	A
ATOM	1270	CD1	ILE	A	306	-5.497	7.343	55.272	1.00	17.56	A
ATOM	1271	C	ILE	A	306	-1.690	4.523	57.076	1.00	15.24	A
ATOM	1272	O	ILE	A	306	-1.898	3.374	56.695	1.00	14.01	A
ATOM	1273	N	PRO	A	307	-1.102	4.774	58.263	1.00	15.58	A
ATOM	1274	CD	PRO	A	307	-0.741	3.622	59.105	1.00	15.34	A
ATOM	1275	CA	PRO	A	307	-0.734	6.032	58.931	1.00	15.50	A
ATOM	1276	CB	PRO	A	307	-0.091	5.558	60.231	1.00	15.22	A
ATOM	1277	CG	PRO	A	307	-0.732	4.223	60.473	1.00	16.17	A
ATOM	1278	C	PRO	A	307	0.233	6.893	58.118	1.00	14.70	A
ATOM	1279	O	PRO	A	307	1.327	6.450	57.770	1.00	14.97	A
ATOM	1280	N	THR	A	308	-0.166	8.127	57.837	1.00	14.00	A
ATOM	1281	CA	THR	A	308	0.670	9.037	57.063	1.00	13.42	A
ATOM	1282	CB	THR	A	308	-0.014	10.400	56.895	1.00	12.26	A
ATOM	1283	OG1	THR	A	308	-1.382	10.200	56.525	1.00	11.53	A
ATOM	1284	CG2	THR	A	308	0.681	11.214	55.811	1.00	11.72	A
ATOM	1285	C	THR	A	308	2.015	9.246	57.744	1.00	13.18	A
ATOM	1286	O	THR	A	308	3.048	9.305	57.084	1.00	12.83	A
ATOM	1287	N	GLU	A	309	1.982	9.366	59.068	1.00	13.59	A
ATOM	1288	CA	GLU	A	309	3.178	9.567	59.879	1.00	16.27	A
ATOM	1289	CB	GLU	A	309	2.800	9.547	61.369	1.00	18.18	A
ATOM	1290	CG	GLU	A	309	3.854	8.954	62.303	1.00	22.15	A
ATOM	1291	CD	GLU	A	309	5.121	9.782	62.391	1.00	25.47	A
ATOM	1292	OE1	GLU	A	309	6.111	9.287	62.974	1.00	27.57	A
ATOM	1293	OE2	GLU	A	309	5.130	10.926	61.890	1.00	26.88	A
ATOM	1294	C	GLU	A	309	4.268	8.531	59.618	1.00	16.07	A
ATOM	1295	O	GLU	A	309	5.455	8.827	59.734	1.00	15.96	A
ATOM	1296	N	ARG	A	310	3.865	7.316	59.275	1.00	17.19	A
ATOM	1297	CA	ARG	A	310	4.831	6.253	59.032	1.00	18.70	A
ATOM	1298	CB	ARG	A	310	4.242	4.898	59.428	1.00	22.99	A
ATOM	1299	CG	ARG	A	310	4.005	4.714	60.917	1.00	28.37	A
ATOM	1300	CD	ARG	A	310	3.387	3.353	61.180	1.00	32.66	A
ATOM	1301	NE	ARG	A	310	3.293	3.045	62.605	1.00	36.84	A
ATOM	1302	CZ	ARG	A	310	2.722	1.948	63.089	1.00	37.07	A
ATOM	1303	NH1	ARG	A	310	2.191	1.057	62.261	1.00	39.09	A
ATOM	1304	NH2	ARG	A	310	2.685	1.739	64.397	1.00	39.15	A
ATOM	1305	C	ARG	A	310	5.308	6.170	57.592	1.00	17.16	A
ATOM	1306	O	ARG	A	310	6.280	5.469	57.303	1.00	17.79	A
ATOM	1307	N	TYR	A	311	4.645	6.883	56.691	1.00	14.11	A
ATOM	1308	CA	TYR	A	311	5.031	6.817	55.285	1.00	13.57	A
ATOM	1309	CB	TYR	A	311	3.943	6.083	54.490	1.00	12.91	A
ATOM	1310	CG	TYR	A	311	3.664	4.697	55.016	1.00	13.42	A
ATOM	1311	CD1	TYR	A	311	2.685	4.482	55.986	1.00	16.46	A
ATOM	1312	CE1	TYR	A	311	2.490	3.224	56.547	1.00	16.91	A
ATOM	1313	CD2	TYR	A	311	4.438	3.615	54.615	1.00	14.44	A
ATOM	1314	CE2	TYR	A	311	4.257	2.360	55.168	1.00	16.71	A
ATOM	1315	CZ	TYR	A	311	3.283	2.169	56.138	1.00	18.56	A
ATOM	1316	OH	TYR	A	311	3.131	0.927	56.718	1.00	21.20	A
ATOM	1317	C	TYR	A	311	5.332	8.157	54.629	1.00	12.97	A
ATOM	1318	O	TYR	A	311	5.315	8.268	53.401	1.00	12.31	A
ATOM	1319	N	PHE	A	312	5.623	9.166	55.443	1.00	12.60	A

ATOM	1320	CA	PHE	A	312	5.917	10.496	54.930	1.00	12.48	A
ATOM	1321	CB	PHE	A	312	4.688	11.402	55.097	1.00	12.89	A
ATOM	1322	CG	PHE	A	312	4.973	12.862	54.860	1.00	13.09	A
ATOM	1323	CD1	PHE	A	312	4.861	13.409	53.585	1.00	11.61	A
ATOM	1324	CD2	PHE	A	312	5.389	13.681	55.907	1.00	12.16	A
ATOM	1325	CE1	PHE	A	312	5.159	14.744	53.353	1.00	12.83	A
ATOM	1326	CE2	PHE	A	312	5.691	15.022	55.685	1.00	13.25	A
ATOM	1327	CZ	PHE	A	312	5.576	15.555	54.402	1.00	13.34	A
ATOM	1328	C	PHE	A	312	7.110	11.150	55.624	1.00	12.93	A
ATOM	1329	O	PHE	A	312	7.212	11.127	56.853	1.00	13.06	A
ATOM	1330	N	PHE	A	313	8.016	11.721	54.833	1.00	12.17	A
ATOM	1331	CA	PHE	A	313	9.168	12.432	55.385	1.00	12.08	A
ATOM	1332	CB	PHE	A	313	10.118	11.466	56.118	1.00	12.85	A
ATOM	1333	CG	PHE	A	313	10.760	10.426	55.244	1.00	14.22	A
ATOM	1334	CD1	PHE	A	313	11.835	10.749	54.428	1.00	14.31	A
ATOM	1335	CD2	PHE	A	313	10.315	9.108	55.274	1.00	14.25	A
ATOM	1336	CE1	PHE	A	313	12.465	9.773	53.656	1.00	15.02	A
ATOM	1337	CE2	PHE	A	313	10.938	8.126	54.505	1.00	14.36	A
ATOM	1338	CZ	PHE	A	313	12.015	8.459	53.695	1.00	13.62	A
ATOM	1339	C	PHE	A	313	9.903	13.257	54.330	1.00	12.75	A
ATOM	1340	O	PHE	A	313	9.659	13.099	53.127	1.00	12.22	A
ATOM	1341	N	ASN	A	314	10.784	14.149	54.785	1.00	11.08	A
ATOM	1342	CA	ASN	A	314	11.543	15.024	53.892	1.00	10.49	A
ATOM	1343	CB	ASN	A	314	12.032	16.250	54.671	1.00	12.41	A
ATOM	1344	CG	ASN	A	314	12.615	17.332	53.771	1.00	11.22	A
ATOM	1345	OD1	ASN	A	314	13.747	17.227	53.308	1.00	12.26	A
ATOM	1346	ND2	ASN	A	314	11.837	18.381	53.526	1.00	10.25	A
ATOM	1347	C	ASN	A	314	12.717	14.293	53.238	1.00	10.74	A
ATOM	1348	O	ASN	A	314	13.433	13.532	53.890	1.00	8.98	A
ATOM	1349	N	VAL	A	315	12.897	14.534	51.940	1.00	10.78	A
ATOM	1350	CA	VAL	A	315	13.952	13.900	51.152	1.00	10.36	A
ATOM	1351	CB	VAL	A	315	13.967	14.458	49.711	1.00	9.40	A
ATOM	1352	CG1	VAL	A	315	14.196	15.962	49.741	1.00	9.49	A
ATOM	1353	CG2	VAL	A	315	15.053	13.774	48.898	1.00	11.21	A
ATOM	1354	C	VAL	A	315	15.354	14.051	51.748	1.00	10.97	A
ATOM	1355	O	VAL	A	315	16.208	13.185	51.566	1.00	11.43	A
ATOM	1356	N	SER	A	316	15.587	15.146	52.460	1.00	12.23	A
ATOM	1357	CA	SER	A	316	16.893	15.403	53.068	1.00	12.04	A
ATOM	1358	CB	SER	A	316	17.167	16.903	53.090	1.00	10.52	A
ATOM	1359	OG	SER	A	316	17.337	17.393	51.771	1.00	16.34	A
ATOM	1360	C	SER	A	316	17.022	14.855	54.481	1.00	11.85	A
ATOM	1361	O	SER	A	316	18.048	15.045	55.131	1.00	10.15	A
ATOM	1362	N	ASP	A	317	15.982	14.171	54.949	1.00	11.31	A
ATOM	1363	CA	ASP	A	317	15.970	13.611	56.299	1.00	10.43	A
ATOM	1364	CB	ASP	A	317	14.572	13.793	56.901	1.00	8.97	A
ATOM	1365	CG	ASP	A	317	14.504	13.410	58.372	1.00	11.08	A
ATOM	1366	OD1	ASP	A	317	13.452	13.672	59.003	1.00	12.28	A
ATOM	1367	OD2	ASP	A	317	15.488	12.844	58.893	1.00	7.73	A
ATOM	1368	C	ASP	A	317	16.364	12.134	56.286	1.00	10.67	A
ATOM	1369	O	ASP	A	317	15.505	11.260	56.203	1.00	11.01	A
ATOM	1370	N	GLU	A	318	17.666	11.863	56.366	1.00	10.77	A
ATOM	1371	CA	GLU	A	318	18.172	10.489	56.351	1.00	12.17	A
ATOM	1372	CB	GLU	A	318	19.696	10.484	56.131	1.00	12.51	A
ATOM	1373	CG	GLU	A	318	20.129	11.110	54.810	1.00	11.53	A
ATOM	1374	CD	GLU	A	318	21.635	11.139	54.623	1.00	12.31	A
ATOM	1375	OE1	GLU	A	318	22.093	11.729	53.627	1.00	13.78	A

ATOM	1376	OE2	GLU	A	318	22.364	10.573	55.462	1.00	13.40	A
ATOM	1377	C	GLU	A	318	17.835	9.698	57.612	1.00	12.49	A
ATOM	1378	O	GLU	A	318	17.821	8.468	57.593	1.00	13.32	A
ATOM	1379	N	ALA	A	319	17.576	10.397	58.712	1.00	13.21	A
ATOM	1380	CA	ALA	A	319	17.231	9.730	59.965	1.00	12.18	A
ATOM	1381	CB	ALA	A	319	17.169	10.737	61.101	1.00	10.58	A
ATOM	1382	C	ALA	A	319	15.878	9.054	59.789	1.00	12.66	A
ATOM	1383	O	ALA	A	319	15.727	7.859	60.056	1.00	13.04	A
ATOM	1384	N	ALA	A	320	14.895	9.826	59.337	1.00	12.52	A
ATOM	1385	CA	ALA	A	320	13.557	9.300	59.109	1.00	11.74	A
ATOM	1386	CB	ALA	A	320	12.618	10.420	58.663	1.00	12.20	A
ATOM	1387	C	ALA	A	320	13.613	8.210	58.050	1.00	10.80	A
ATOM	1388	O	ALA	A	320	12.840	7.259	58.095	1.00	11.42	A
ATOM	1389	N	LEU	A	321	14.519	8.351	57.086	1.00	12.37	A
ATOM	1390	CA	LEU	A	321	14.663	7.341	56.033	1.00	11.66	A
ATOM	1391	CB	LEU	A	321	15.769	7.737	55.049	1.00	11.52	A
ATOM	1392	CG	LEU	A	321	16.168	6.650	54.039	1.00	11.08	A
ATOM	1393	CD1	LEU	A	321	14.991	6.348	53.135	1.00	11.70	A
ATOM	1394	CD2	LEU	A	321	17.374	7.100	53.224	1.00	9.59	A
ATOM	1395	C	LEU	A	321	14.996	5.979	56.647	1.00	12.69	A
ATOM	1396	O	LEU	A	321	14.381	4.963	56.313	1.00	11.66	A
ATOM	1397	N	LEU	A	322	15.984	5.958	57.539	1.00	14.23	A
ATOM	1398	CA	LEU	A	322	16.382	4.720	58.201	1.00	13.49	A
ATOM	1399	CB	LEU	A	322	17.680	4.922	58.983	1.00	14.50	A
ATOM	1400	CG	LEU	A	322	19.004	4.955	58.223	1.00	13.92	A
ATOM	1401	CD1	LEU	A	322	20.113	5.395	59.171	1.00	14.87	A
ATOM	1402	CD2	LEU	A	322	19.297	3.564	57.643	1.00	13.58	A
ATOM	1403	C	LEU	A	322	15.296	4.255	59.165	1.00	15.38	A
ATOM	1404	O	LEU	A	322	15.114	3.054	59.381	1.00	15.20	A
ATOM	1405	N	GLU	A	323	14.578	5.210	59.747	1.00	15.18	A
ATOM	1406	CA	GLU	A	323	13.518	4.887	60.693	1.00	18.29	A
ATOM	1407	CB	GLU	A	323	13.138	6.116	61.518	1.00	18.66	A
ATOM	1408	CG	GLU	A	323	12.001	5.857	62.490	1.00	21.49	A
ATOM	1409	CD	GLU	A	323	11.437	7.128	63.089	1.00	24.28	A
ATOM	1410	OE1	GLU	A	323	10.674	7.831	62.393	1.00	22.67	A
ATOM	1411	OE2	GLU	A	323	11.765	7.429	64.259	1.00	27.85	A
ATOM	1412	C	GLU	A	323	12.257	4.365	60.026	1.00	18.63	A
ATOM	1413	O	GLU	A	323	11.669	3.392	60.479	1.00	19.52	A
ATOM	1414	N	LYS	A	324	11.843	5.022	58.952	1.00	20.07	A
ATOM	1415	CA	LYS	A	324	10.620	4.646	58.264	1.00	21.79	A
ATOM	1416	CB	LYS	A	324	9.922	5.917	57.780	1.00	21.00	A
ATOM	1417	CG	LYS	A	324	9.671	6.890	58.926	1.00	21.15	A
ATOM	1418	CD	LYS	A	324	8.868	8.113	58.522	1.00	20.19	A
ATOM	1419	CE	LYS	A	324	8.583	8.984	59.741	1.00	20.66	A
ATOM	1420	NZ	LYS	A	324	7.690	10.134	59.411	1.00	23.09	A
ATOM	1421	C	LYS	A	324	10.791	3.645	57.126	1.00	23.43	A
ATOM	1422	O	LYS	A	324	10.040	2.678	57.043	1.00	23.83	A
ATOM	1423	N	ALA	A	325	11.770	3.869	56.254	1.00	25.84	A
ATOM	1424	CA	ALA	A	325	12.021	2.961	55.138	1.00	27.84	A
ATOM	1425	CB	ALA	A	325	12.364	3.746	53.890	1.00	26.82	A
ATOM	1426	C	ALA	A	325	13.175	2.044	55.510	1.00	30.67	A
ATOM	1427	O	ALA	A	325	13.892	1.541	54.647	1.00	32.48	A
ATOM	1428	N	GLY	A	326	13.346	1.839	56.811	1.00	33.73	A
ATOM	1429	CA	GLY	A	326	14.417	0.997	57.314	1.00	36.36	A
ATOM	1430	C	GLY	A	326	14.545	-0.348	56.630	1.00	37.69	A
ATOM	1431	OT1	GLY	A	326	14.039	-1.339	57.197	1.00	38.55	A

```
ATOM   1432  OT2 GLY A 326      15.140  -0.415  55.530  1.00 38.84      A
TER
ATOM   1433  C   GLY B   1      27.024  31.838  46.808  1.00 46.99      CA
ATOM   1434  O   GLY B   1      25.970  32.170  47.352  1.00 47.64      CA
ATOM   1435  N   GLY B   1      28.053  29.559  47.038  1.00 48.37      CA
ATOM   1436  CA  GLY B   1      28.019  30.960  47.548  1.00 47.58      CA
ATOM   1437  N   PRO B   2      27.344  32.250  45.570  1.00 45.71      CA
ATOM   1438  CD  PRO B   2      28.729  32.222  45.063  1.00 45.50      CA
ATOM   1439  CA  PRO B   2      26.500  33.098  44.719  1.00 44.55      CA
ATOM   1440  CB  PRO B   2      27.520  34.005  44.055  1.00 44.60      CA
ATOM   1441  CG  PRO B   2      28.640  33.039  43.793  1.00 45.19      CA
ATOM   1442  C   PRO B   2      25.681  32.303  43.689  1.00 42.88      CA
ATOM   1443  O   PRO B   2      26.113  32.125  42.547  1.00 43.57      CA
ATOM   1444  N   HYP B   3      24.480  31.829  44.077  1.00 40.90      CA
ATOM   1445  CD  HYP B   3      23.853  31.959  45.404  1.00 39.90      CA
ATOM   1446  CA  HYP B   3      23.620  31.053  43.172  1.00 37.74      CA
ATOM   1447  CB  HYP B   3      22.372  30.790  44.019  1.00 38.68      CA
ATOM   1448  CG  HYP B   3      22.917  30.779  45.414  1.00 39.07      CA
ATOM   1449  C   HYP B   3      23.287  31.766  41.864  1.00 34.90      CA
ATOM   1450  O   HYP B   3      23.009  32.965  41.852  1.00 34.40      CA
ATOM   1451  OD  HYP B   3      21.922  30.851  46.427  1.00 38.93      CA
ATOM   1452  N   GLY B   4      23.312  31.014  40.767  1.00 30.95      CA
ATOM   1453  CA  GLY B   4      23.008  31.583  39.470  1.00 26.85      CA
ATOM   1454  C   GLY B   4      21.622  32.197  39.402  1.00 24.34      CA
ATOM   1455  O   GLY B   4      20.841  32.078  40.344  1.00 23.22      CA
ATOM   1456  N   PRO B   5      21.286  32.870  38.295  1.00 22.36      CA
ATOM   1457  CD  PRO B   5      22.104  33.084  37.086  1.00 22.48      CA
ATOM   1458  CA  PRO B   5      19.966  33.493  38.150  1.00 21.43      CA
ATOM   1459  CB  PRO B   5      20.144  34.374  36.920  1.00 22.25      CA
ATOM   1460  CG  PRO B   5      21.075  33.559  36.076  1.00 23.04      CA
ATOM   1461  C   PRO B   5      18.867  32.455  37.959  1.00 19.31      CA
ATOM   1462  O   PRO B   5      19.131  31.347  37.498  1.00 17.49      CA
ATOM   1463  N   HYP B   6      17.619  32.798  38.320  1.00 18.67      CA
ATOM   1464  CD  HYP B   6      17.170  34.008  39.031  1.00 18.03      CA
ATOM   1465  CA  HYP B   6      16.516  31.841  38.152  1.00 17.47      CA
ATOM   1466  CB  HYP B   6      15.343  32.512  38.872  1.00 18.15      CA
ATOM   1467  CG  HYP B   6      16.002  33.485  39.813  1.00 17.95      CA
ATOM   1468  C   HYP B   6      16.223  31.664  36.666  1.00 17.02      CA
ATOM   1469  O   HYP B   6      16.597  32.516  35.851  1.00 13.78      CA
ATOM   1470  OD  HYP B   6      16.366  32.917  41.063  1.00 17.03      CA
ATOM   1471  N   GLY B   7      15.554  30.567  36.315  1.00 16.69      CA
ATOM   1472  CA  GLY B   7      15.211  30.333  34.921  1.00 17.54      CA
ATOM   1473  C   GLY B   7      14.116  31.297  34.496  1.00 18.10      CA
ATOM   1474  O   GLY B   7      13.595  32.034  35.331  1.00 18.65      CA
ATOM   1475  N   PHE B   8      13.768  31.308  33.211  1.00 18.05      CA
ATOM   1476  CA  PHE B   8      12.724  32.201  32.719  1.00 20.44      CA
ATOM   1477  CB  PHE B   8      12.758  32.294  31.191  1.00 24.57      CA
ATOM   1478  CG  PHE B   8      13.366  33.569  30.675  1.00 28.99      CA
ATOM   1479  CD1 PHE B   8      14.744  33.782  30.745  1.00 31.01      CA
ATOM   1480  CD2 PHE B   8      12.559  34.566  30.132  1.00 30.61      CA
ATOM   1481  CE1 PHE B   8      15.310  34.969  30.276  1.00 31.21      CA
ATOM   1482  CE2 PHE B   8      13.112  35.753  29.662  1.00 33.13      CA
ATOM   1483  CZ  PHE B   8      14.494  35.956  29.735  1.00 33.64      CA
ATOM   1484  C   PHE B   8      11.334  31.758  33.160  1.00 20.03      CA
ATOM   1485  O   PHE B   8      11.090  30.575  33.386  1.00 21.24      CA
ATOM   1486  N   HYP B   9      10.401  32.714  33.285  1.00 19.18      CA
```

ATOM	1487	CD	HYP	B	9	10.596	34.152	33.031	1.00	19.09	CA
ATOM	1488	CA	HYP	B	9	9.023	32.425	33.704	1.00	18.49	CA
ATOM	1489	CB	HYP	B	9	8.354	33.804	33.689	1.00	18.16	CA
ATOM	1490	CG	HYP	B	9	9.528	34.762	33.877	1.00	19.48	CA
ATOM	1491	C	HYP	B	9	8.338	31.436	32.754	1.00	17.86	CA
ATOM	1492	O	HYP	B	9	8.523	31.503	31.539	1.00	16.69	CA
ATOM	1493	OD	HYP	B	9	9.934	34.942	35.228	1.00	19.21	CA
ATOM	1494	N	GLY	B	10	7.549	30.523	33.315	1.00	18.32	CA
ATOM	1495	CA	GLY	B	10	6.853	29.534	32.510	1.00	16.17	CA
ATOM	1496	C	GLY	B	10	5.674	30.093	31.732	1.00	17.31	CA
ATOM	1497	O	GLY	B	10	5.255	31.237	31.942	1.00	16.56	CA
ATOM	1498	N	GLU	B	11	5.127	29.273	30.839	1.00	18.09	CA
ATOM	1499	CA	GLU	B	11	4.001	29.678	30.009	1.00	19.81	CA
ATOM	1500	CB	GLU	B	11	4.092	29.010	28.631	1.00	23.10	CA
ATOM	1501	CG	GLU	B	11	5.378	29.311	27.853	1.00	27.78	CA
ATOM	1502	CD	GLU	B	11	5.602	30.797	27.595	1.00	31.41	CA
ATOM	1503	OE1	GLU	B	11	6.604	31.130	26.918	1.00	33.15	CA
ATOM	1504	OE2	GLU	B	11	4.791	31.631	28.065	1.00	32.81	CA
ATOM	1505	C	GLU	B	11	2.644	29.363	30.633	1.00	19.40	CA
ATOM	1506	O	GLU	B	11	2.560	28.777	31.715	1.00	17.55	CA
ATOM	1507	N	ARG	B	12	1.590	29.763	29.927	1.00	18.86	CA
ATOM	1508	CA	ARG	B	12	0.205	29.562	30.345	1.00	17.24	CA
ATOM	1509	CB	ARG	B	12	-0.716	30.084	29.241	1.00	20.84	CA
ATOM	1510	CG	ARG	B	12	-2.198	29.983	29.527	1.00	24.57	CA
ATOM	1511	CD	ARG	B	12	-3.024	30.038	28.231	1.00	28.77	CA
ATOM	1512	NE	ARG	B	12	-2.686	31.166	27.361	1.00	30.12	CA
ATOM	1513	CZ	ARG	B	12	-1.675	31.176	26.496	1.00	30.49	CA
ATOM	1514	NH1	ARG	B	12	-0.889	30.115	26.372	1.00	32.79	CA
ATOM	1515	NH2	ARG	B	12	-1.441	32.249	25.756	1.00	29.66	CA
ATOM	1516	C	ARG	B	12	-0.100	28.080	30.613	1.00	15.45	CA
ATOM	1517	O	ARG	B	12	0.424	27.194	29.939	1.00	13.71	CA
ATOM	1518	N	GLY	B	13	-0.961	27.818	31.588	1.00	13.54	CA
ATOM	1519	CA	GLY	B	13	-1.306	26.445	31.911	1.00	13.61	CA
ATOM	1520	C	GLY	B	13	-2.249	25.800	30.908	1.00	14.71	CA
ATOM	1521	O	GLY	B	13	-2.823	26.492	30.060	1.00	12.72	CA
ATOM	1522	N	PRO	B	14	-2.421	24.464	30.969	1.00	15.39	CA
ATOM	1523	CD	PRO	B	14	-1.663	23.508	31.797	1.00	14.36	CA
ATOM	1524	CA	PRO	B	14	-3.315	23.753	30.047	1.00	14.99	CA
ATOM	1525	CB	PRO	B	14	-3.052	22.279	30.369	1.00	14.60	CA
ATOM	1526	CG	PRO	B	14	-1.631	22.288	30.905	1.00	15.31	CA
ATOM	1527	C	PRO	B	14	-4.775	24.130	30.301	1.00	15.89	CA
ATOM	1528	O	PRO	B	14	-5.107	24.718	31.335	1.00	15.18	CA
ATOM	1529	N	HYP	B	15	-5.668	23.795	29.357	1.00	16.77	CA
ATOM	1530	CD	HYP	B	15	-5.431	23.164	28.046	1.00	15.95	CA
ATOM	1531	CA	HYP	B	15	-7.084	24.123	29.546	1.00	17.68	CA
ATOM	1532	CB	HYP	B	15	-7.709	23.788	28.191	1.00	18.28	CA
ATOM	1533	CG	HYP	B	15	-6.821	22.717	27.647	1.00	16.55	CA
ATOM	1534	C	HYP	B	15	-7.689	23.310	30.683	1.00	19.44	CA
ATOM	1535	O	HYP	B	15	-7.169	22.259	31.053	1.00	18.88	CA
ATOM	1536	OD	HYP	B	15	-6.966	22.530	26.236	1.00	17.79	CA
ATOM	1537	N	GLY	B	16	-8.785	23.810	31.239	1.00	20.37	CA
ATOM	1538	CA	GLY	B	16	-9.434	23.116	32.333	1.00	21.79	CA
ATOM	1539	C	GLY	B	16	-10.233	21.920	31.862	1.00	22.72	CA
ATOM	1540	O	GLY	B	16	-10.466	21.755	30.661	1.00	22.43	CA
ATOM	1541	N	PRO	B	17	-10.666	21.057	32.792	1.00	24.17	CA
ATOM	1542	CD	PRO	B	17	-10.472	21.137	34.252	1.00	24.95	CA

```
ATOM   1543  CA  PRO B  17     -11.446  19.874  32.434  1.00 26.22      CA
ATOM   1544  CB  PRO B  17     -11.562  19.126  33.758  1.00 26.53      CA
ATOM   1545  CG  PRO B  17     -11.556  20.225  34.768  1.00 25.15      CA
ATOM   1546  C   PRO B  17     -12.803  20.235  31.847  1.00 27.93      CA
ATOM   1547  O   PRO B  17     -13.339  21.315  32.107  1.00 27.72      CA
ATOM   1548  N   HYP B  18     -13.371  19.335  31.032  1.00 29.77      CA
ATOM   1549  CD  HYP B  18     -12.833  18.023  30.625  1.00 29.92      CA
ATOM   1550  CA  HYP B  18     -14.679  19.591  30.420  1.00 30.56      CA
ATOM   1551  CB  HYP B  18     -15.021  18.263  29.747  1.00 30.75      CA
ATOM   1552  CG  HYP B  18     -13.678  17.690  29.426  1.00 30.63      CA
ATOM   1553  C   HYP B  18     -15.705  19.957  31.477  1.00 31.35      CA
ATOM   1554  O   HYP B  18     -15.523  19.677  32.662  1.00 32.13      CA
ATOM   1555  OD  HYP B  18     -13.134  18.149  28.197  1.00 31.27      CA
ATOM   1556  N   GLY B  19     -16.780  20.603  31.051  1.00 32.29      CA
ATOM   1557  CA  GLY B  19     -17.829  20.951  31.990  1.00 32.48      CA
ATOM   1558  C   GLY B  19     -18.840  19.817  31.903  1.00 33.06      CA
ATOM   1559  O   GLY B  19     -18.815  19.070  30.926  1.00 31.96      CA
ATOM   1560  N   PRO B  20     -19.723  19.649  32.896  1.00 34.64      CA
ATOM   1561  CD  PRO B  20     -19.991  20.482  34.080  1.00 34.66      CA
ATOM   1562  CA  PRO B  20     -20.694  18.555  32.792  1.00 34.86      CA
ATOM   1563  CB  PRO B  20     -21.571  18.748  34.025  1.00 34.62      CA
ATOM   1564  CG  PRO B  20     -21.457  20.218  34.307  1.00 35.11      CA
ATOM   1565  C   PRO B  20     -21.476  18.610  31.477  1.00 35.93      CA
ATOM   1566  O   PRO B  20     -21.684  19.689  30.917  1.00 35.62      CA
ATOM   1567  N   HYP B  21     -21.915  17.443  30.973  1.00 36.92      CA
ATOM   1568  CD  HYP B  21     -21.636  16.123  31.566  1.00 37.42      CA
ATOM   1569  CA  HYP B  21     -22.684  17.306  29.723  1.00 37.36      CA
ATOM   1570  CB  HYP B  21     -23.146  15.844  29.760  1.00 37.79      CA
ATOM   1571  CG  HYP B  21     -22.011  15.169  30.442  1.00 38.04      CA
ATOM   1572  C   HYP B  21     -23.851  18.280  29.636  1.00 37.37      CA
ATOM   1573  O   HYP B  21     -24.393  18.515  28.554  1.00 37.88      CA
ATOM   1574  OD  HYP B  21     -20.938  14.807  29.569  1.00 39.73      CA
ATOM   1575  N   NHH B  22     -24.252  18.843  30.764  1.00 37.11      CA
TER
ATOM   1576  C   GLY C   1      35.293  30.667  43.820  1.00 42.71      CB
ATOM   1577  O   GLY C   1      35.319  30.946  42.621  1.00 42.96      CB
ATOM   1578  N   GLY C   1      35.242  32.981  44.701  1.00 43.02      CB
ATOM   1579  CA  GLY C   1      35.861  31.634  44.838  1.00 42.85      CB
ATOM   1580  N   PRO C   2      34.789  29.507  44.263  1.00 42.50      CB
ATOM   1581  CD  PRO C   2      34.909  28.933  45.614  1.00 42.71      CB
ATOM   1582  CA  PRO C   2      34.218  28.530  43.333  1.00 41.69      CB
ATOM   1583  CB  PRO C   2      33.847  27.366  44.247  1.00 42.23      CB
ATOM   1584  CG  PRO C   2      34.875  27.450  45.329  1.00 42.25      CB
ATOM   1585  C   PRO C   2      32.993  29.123  42.640  1.00 41.38      CB
ATOM   1586  O   PRO C   2      32.420  30.109  43.113  1.00 40.38      CB
ATOM   1587  N   HYP C   3      32.576  28.538  41.506  1.00 41.08      CB
ATOM   1588  CD  HYP C   3      33.085  27.350  40.795  1.00 41.06      CB
ATOM   1589  CA  HYP C   3      31.395  29.105  40.841  1.00 39.79      CB
ATOM   1590  CB  HYP C   3      31.311  28.320  39.532  1.00 40.33      CB
ATOM   1591  CG  HYP C   3      31.925  26.997  39.886  1.00 41.40      CB
ATOM   1592  C   HYP C   3      30.151  28.938  41.710  1.00 38.06      CB
ATOM   1593  O   HYP C   3      30.065  28.007  42.517  1.00 36.78      CB
ATOM   1594  OD  HYP C   3      31.010  26.058  40.447  1.00 40.66      CB
ATOM   1595  N   GLY C   4      29.199  29.851  41.550  1.00 36.06      CB
ATOM   1596  CA  GLY C   4      27.978  29.787  42.330  1.00 33.48      CB
ATOM   1597  C   GLY C   4      27.149  28.549  42.031  1.00 31.26      CB
```

```
ATOM   1598  O   GLY C   4      27.274  27.958  40.957  1.00 29.93      CB
ATOM   1599  N   PRO C   5      26.288  28.130  42.972  1.00 29.27      CB
ATOM   1600  CD  PRO C   5      25.996  28.786  44.260  1.00 29.55      CB
ATOM   1601  CA  PRO C   5      25.439  26.951  42.789  1.00 27.57      CB
ATOM   1602  CB  PRO C   5      24.900  26.705  44.190  1.00 29.16      CB
ATOM   1603  CG  PRO C   5      24.708  28.101  44.691  1.00 29.18      CB
ATOM   1604  C   PRO C   5      24.325  27.240  41.782  1.00 24.50      CB
ATOM   1605  O   PRO C   5      23.970  28.397  41.554  1.00 23.77      CB
ATOM   1606  N   HYP C   6      23.769  26.190  41.162  1.00 23.07      CB
ATOM   1607  CD  HYP C   6      24.191  24.781  41.263  1.00 23.05      CB
ATOM   1608  CA  HYP C   6      22.693  26.336  40.177  1.00 22.11      CB
ATOM   1609  CB  HYP C   6      22.223  24.903  39.975  1.00 22.93      CB
ATOM   1610  CG  HYP C   6      23.502  24.157  40.067  1.00 24.04      CB
ATOM   1611  C   HYP C   6      21.562  27.253  40.621  1.00 20.21      CB
ATOM   1612  O   HYP C   6      21.185  27.275  41.790  1.00 19.92      CB
ATOM   1613  OD  HYP C   6      24.272  24.224  38.878  1.00 25.59      CB
ATOM   1614  N   GLY C   7      21.020  28.004  39.673  1.00 18.24      CB
ATOM   1615  CA  GLY C   7      19.929  28.908  39.982  1.00 18.08      CB
ATOM   1616  C   GLY C   7      18.631  28.158  40.205  1.00 16.18      CB
ATOM   1617  O   GLY C   7      18.453  27.058  39.687  1.00 15.68      CB
ATOM   1618  N   PHE C   8      17.736  28.753  40.991  1.00 16.45      CB
ATOM   1619  CA  PHE C   8      16.433  28.162  41.297  1.00 15.97      CB
ATOM   1620  CB  PHE C   8      15.684  29.024  42.326  1.00 19.10      CB
ATOM   1621  CG  PHE C   8      16.405  29.201  43.641  1.00 22.85      CB
ATOM   1622  CD1 PHE C   8      17.639  29.847  43.705  1.00 25.50      CB
ATOM   1623  CD2 PHE C   8      15.823  28.769  44.827  1.00 25.25      CB
ATOM   1624  CE1 PHE C   8      18.275  30.069  44.936  1.00 26.15      CB
ATOM   1625  CE2 PHE C   8      16.450  28.984  46.062  1.00 26.74      CB
ATOM   1626  CZ  PHE C   8      17.676  29.634  46.115  1.00 25.84      CB
ATOM   1627  C   PHE C   8      15.580  28.067  40.025  1.00 13.88      CB
ATOM   1628  O   PHE C   8      15.840  28.758  39.043  1.00  9.98      CB
ATOM   1629  N   HYP C   9      14.556  27.192  40.026  1.00 13.66      CB
ATOM   1630  CD  HYP C   9      14.269  26.169  41.046  1.00 12.78      CB
ATOM   1631  CA  HYP C   9      13.678  27.034  38.858  1.00 12.96      CB
ATOM   1632  CB  HYP C   9      12.718  25.924  39.289  1.00 13.91      CB
ATOM   1633  CG  HYP C   9      13.551  25.116  40.242  1.00 14.02      CB
ATOM   1634  C   HYP C   9      12.943  28.350  38.612  1.00 12.77      CB
ATOM   1635  O   HYP C   9      12.730  29.123  39.543  1.00 12.44      CB
ATOM   1636  OD  HYP C   9      14.426  24.210  39.593  1.00 14.70      CB
ATOM   1637  N   GLY C  10      12.557  28.607  37.369  1.00 11.71      CB
ATOM   1638  CA  GLY C  10      11.855  29.845  37.076  1.00 13.31      CB
ATOM   1639  C   GLY C  10      10.401  29.830  37.520  1.00 13.58      CB
ATOM   1640  O   GLY C  10       9.823  28.767  37.734  1.00 13.71      CB
ATOM   1641  N   GLU C  11       9.814  31.015  37.667  1.00 14.37      CB
ATOM   1642  CA  GLU C  11       8.422  31.147  38.076  1.00 15.28      CB
ATOM   1643  CB  GLU C  11       7.982  32.612  37.999  1.00 16.41      CB
ATOM   1644  CG  GLU C  11       8.639  33.530  39.015  1.00 16.23      CB
ATOM   1645  CD  GLU C  11       8.383  33.087  40.441  1.00 16.67      CB
ATOM   1646  OE1 GLU C  11       9.296  32.503  41.064  1.00 18.10      CB
ATOM   1647  OE2 GLU C  11       7.262  33.310  40.935  1.00 17.35      CB
ATOM   1648  C   GLU C  11       7.505  30.313  37.187  1.00 15.50      CB
ATOM   1649  O   GLU C  11       7.720  30.211  35.979  1.00 13.06      CB
ATOM   1650  N   ARG C  12       6.480  29.719  37.793  1.00 17.27      CB
ATOM   1651  CA  ARG C  12       5.523  28.903  37.054  1.00 18.14      CB
ATOM   1652  CB  ARG C  12       4.729  28.023  38.020  1.00 20.84      CB
ATOM   1653  CG  ARG C  12       3.932  26.932  37.347  1.00 23.28      CB
```

```
ATOM   1654  CD  ARG C  12       3.098  26.164  38.356  1.00 25.19      CB
ATOM   1655  NE  ARG C  12       2.324  25.099  37.725  1.00 25.98      CB
ATOM   1656  CZ  ARG C  12       1.444  24.341  38.371  1.00 27.02      CB
ATOM   1657  NH1 ARG C  12       1.229  24.535  39.665  1.00 26.61      CB
ATOM   1658  NH2 ARG C  12       0.780  23.390  37.728  1.00 26.52      CB
ATOM   1659  C   ARG C  12       4.586  29.843  36.299  1.00 18.11      CB
ATOM   1660  O   ARG C  12       4.235  30.912  36.807  1.00 18.92      CB
ATOM   1661  N   GLY C  13       4.198  29.459  35.086  1.00 16.77      CB
ATOM   1662  CA  GLY C  13       3.317  30.300  34.297  1.00 15.62      CB
ATOM   1663  C   GLY C  13       2.003  30.595  34.998  1.00 16.24      CB
ATOM   1664  O   GLY C  13       1.769  30.107  36.105  1.00 15.03      CB
ATOM   1665  N   PRO C  14       1.128  31.412  34.388  1.00 16.73      CB
ATOM   1666  CD  PRO C  14       1.348  32.224  33.174  1.00 16.28      CB
ATOM   1667  CA  PRO C  14      -0.162  31.736  35.007  1.00 16.91      CB
ATOM   1668  CB  PRO C  14      -0.526  33.065  34.359  1.00 17.54      CB
ATOM   1669  CG  PRO C  14      -0.009  32.879  32.957  1.00 17.17      CB
ATOM   1670  C   PRO C  14      -1.190  30.646  34.702  1.00 16.45      CB
ATOM   1671  O   PRO C  14      -0.983  29.820  33.820  1.00 13.87      CB
ATOM   1672  N   HYP C  15      -2.313  30.637  35.433  1.00 17.28      CB
ATOM   1673  CD  HYP C  15      -2.597  31.470  36.615  1.00 17.85      CB
ATOM   1674  CA  HYP C  15      -3.370  29.639  35.224  1.00 16.58      CB
ATOM   1675  CB  HYP C  15      -4.470  30.097  36.174  1.00 18.24      CB
ATOM   1676  CG  HYP C  15      -3.696  30.684  37.300  1.00 18.18      CB
ATOM   1677  C   HYP C  15      -3.863  29.580  33.784  1.00 15.70      CB
ATOM   1678  O   HYP C  15      -4.031  30.612  33.137  1.00 15.03      CB
ATOM   1679  OD  HYP C  15      -3.209  29.719  38.215  1.00 19.41      CB
ATOM   1680  N   GLY C  16      -4.088  28.363  33.292  1.00 15.59      CB
ATOM   1681  CA  GLY C  16      -4.586  28.171  31.943  1.00 12.51      CB
ATOM   1682  C   GLY C  16      -6.038  28.619  31.839  1.00 13.38      CB
ATOM   1683  O   GLY C  16      -6.658  28.942  32.861  1.00 10.23      CB
ATOM   1684  N   PRO C  17      -6.616  28.637  30.624  1.00 12.36      CB
ATOM   1685  CD  PRO C  17      -5.984  28.233  29.354  1.00 12.72      CB
ATOM   1686  CA  PRO C  17      -8.003  29.056  30.396  1.00 13.23      CB
ATOM   1687  CB  PRO C  17      -8.023  29.337  28.900  1.00 14.02      CB
ATOM   1688  CG  PRO C  17      -7.154  28.252  28.377  1.00 10.82      CB
ATOM   1689  C   PRO C  17      -9.041  28.003  30.791  1.00 13.57      CB
ATOM   1690  O   PRO C  17      -8.714  26.821  30.965  1.00 11.15      CB
ATOM   1691  N   HYP C  18     -10.313  28.425  30.926  1.00 12.83      CB
ATOM   1692  CD  HYP C  18     -10.797  29.804  30.744  1.00 11.99      CB
ATOM   1693  CA  HYP C  18     -11.418  27.532  31.298  1.00 13.95      CB
ATOM   1694  CB  HYP C  18     -12.636  28.460  31.291  1.00 11.62      CB
ATOM   1695  CG  HYP C  18     -12.048  29.793  31.565  1.00 12.88      CB
ATOM   1696  C   HYP C  18     -11.569  26.406  30.279  1.00 14.31      CB
ATOM   1697  O   HYP C  18     -11.328  26.611  29.093  1.00 15.44      CB
ATOM   1698  OD  HYP C  18     -11.810  30.040  32.943  1.00 13.37      CB
ATOM   1699  N   GLY C  19     -11.968  25.227  30.742  1.00 14.55      CB
ATOM   1700  CA  GLY C  19     -12.143  24.102  29.846  1.00 13.79      CB
ATOM   1701  C   GLY C  19     -13.352  24.277  28.942  1.00 14.74      CB
ATOM   1702  O   GLY C  19     -14.112  25.234  29.098  1.00 13.65      CB
ATOM   1703  N   PRO C  20     -13.564  23.368  27.980  1.00 15.70      CB
ATOM   1704  CD  PRO C  20     -12.694  22.250  27.562  1.00 15.16      CB
ATOM   1705  CA  PRO C  20     -14.725  23.500  27.093  1.00 16.72      CB
ATOM   1706  CB  PRO C  20     -14.347  22.622  25.912  1.00 15.89      CB
ATOM   1707  CG  PRO C  20     -13.562  21.518  26.567  1.00 17.28      CB
ATOM   1708  C   PRO C  20     -16.004  23.036  27.774  1.00 17.49      CB
ATOM   1709  O   PRO C  20     -15.962  22.474  28.870  1.00 18.83      CB
```

```
ATOM   1710  N   HYP C  21     -17.171  23.285  27.139  1.00 18.90      CB
ATOM   1711  CD  HYP C  21     -17.323  24.107  25.924  1.00 20.00      CB
ATOM   1712  CA  HYP C  21     -18.489  22.895  27.667  1.00 19.37      CB
ATOM   1713  CB  HYP C  21     -19.455  23.295  26.540  1.00 20.77      CB
ATOM   1714  CG  HYP C  21     -18.797  24.467  25.957  1.00 19.53      CB
ATOM   1715  C   HYP C  21     -18.536  21.401  27.950  1.00 20.63      CB
ATOM   1716  O   HYP C  21     -17.942  20.627  27.218  1.00 20.57      CB
ATOM   1717  OD  HYP C  21     -19.098  25.673  26.637  1.00 21.66      CB
ATOM   1718  N   NHH C  22     -19.227  20.988  29.001  1.00 19.10      CB
TER
ATOM   1719  C   GLY D   1      31.268  34.798  43.143  1.00 52.14      CC
ATOM   1720  O   GLY D   1      30.268  35.506  43.021  1.00 52.89      CC
ATOM   1721  N   GLY D   1      31.780  33.147  44.952  1.00 53.28      CC
ATOM   1722  CA  GLY D   1      31.873  34.570  44.517  1.00 52.57      CC
ATOM   1723  N   PRO D   2      31.857  34.209  42.087  1.00 51.43      CC
ATOM   1724  CD  PRO D   2      33.111  33.443  42.215  1.00 51.55      CC
ATOM   1725  CA  PRO D   2      31.448  34.287  40.676  1.00 50.79      CC
ATOM   1726  CB  PRO D   2      32.376  33.279  40.005  1.00 51.06      CC
ATOM   1727  CG  PRO D   2      33.628  33.426  40.796  1.00 51.42      CC
ATOM   1728  C   PRO D   2      29.960  33.984  40.413  1.00 49.69      CC
ATOM   1729  O   PRO D   2      29.157  33.928  41.336  1.00 49.54      CC
ATOM   1730  N   HYP D   3      29.577  33.803  39.135  1.00 48.62      CC
ATOM   1731  CD  HYP D   3      30.283  34.328  37.950  1.00 48.82      CC
ATOM   1732  CA  HYP D   3      28.171  33.508  38.814  1.00 46.31      CC
ATOM   1733  CB  HYP D   3      27.945  34.309  37.538  1.00 47.40      CC
ATOM   1734  CG  HYP D   3      29.259  34.142  36.847  1.00 48.30      CC
ATOM   1735  C   HYP D   3      27.806  32.037  38.623  1.00 43.31      CC
ATOM   1736  O   HYP D   3      28.461  31.308  37.872  1.00 43.51      CC
ATOM   1737  OD  HYP D   3      29.400  32.904  36.166  1.00 49.71      CC
ATOM   1738  N   GLY D   4      26.746  31.608  39.301  1.00 40.44      CC
ATOM   1739  CA  GLY D   4      26.299  30.234  39.171  1.00 36.00      CC
ATOM   1740  C   GLY D   4      25.518  30.054  37.881  1.00 32.49      CC
ATOM   1741  O   GLY D   4      25.111  31.040  37.265  1.00 31.46      CC
ATOM   1742  N   PRO D   5      25.300  28.809  37.433  1.00 30.10      CC
ATOM   1743  CD  PRO D   5      25.830  27.545  37.974  1.00 30.57      CC
ATOM   1744  CA  PRO D   5      24.553  28.569  36.197  1.00 27.85      CC
ATOM   1745  CB  PRO D   5      24.874  27.112  35.883  1.00 28.49      CC
ATOM   1746  CG  PRO D   5      25.011  26.512  37.237  1.00 29.90      CC
ATOM   1747  C   PRO D   5      23.051  28.822  36.347  1.00 25.42      CC
ATOM   1748  O   PRO D   5      22.496  28.711  37.440  1.00 24.50      CC
ATOM   1749  N   HYP D   6      22.378  29.174  35.240  1.00 23.36      CC
ATOM   1750  CD  HYP D   6      22.987  29.406  33.920  1.00 22.17      CC
ATOM   1751  CA  HYP D   6      20.935  29.453  35.210  1.00 21.50      CC
ATOM   1752  CB  HYP D   6      20.696  29.920  33.771  1.00 21.57      CC
ATOM   1753  CG  HYP D   6      22.059  30.432  33.343  1.00 23.24      CC
ATOM   1754  C   HYP D   6      20.116  28.209  35.546  1.00 19.47      CC
ATOM   1755  O   HYP D   6      20.454  27.110  35.120  1.00 19.29      CC
ATOM   1756  OD  HYP D   6      22.348  31.750  33.794  1.00 24.53      CC
ATOM   1757  N   GLY D   7      19.044  28.381  36.309  1.00 17.93      CC
ATOM   1758  CA  GLY D   7      18.216  27.240  36.666  1.00 17.76      CC
ATOM   1759  C   GLY D   7      17.295  26.813  35.535  1.00 16.59      CC
ATOM   1760  O   GLY D   7      17.386  27.333  34.422  1.00 14.21      CC
ATOM   1761  N   PHE D   8      16.415  25.854  35.804  1.00 16.53      CC
ATOM   1762  CA  PHE D   8      15.476  25.406  34.778  1.00 15.90      CC
ATOM   1763  CB  PHE D   8      14.733  24.132  35.199  1.00 14.16      CC
ATOM   1764  CG  PHE D   8      15.528  22.869  35.040  1.00 12.37      CC
```

```
ATOM   1765  CD1 PHE D   8      16.339  22.405  36.070  1.00 12.14      CC
ATOM   1766  CD2 PHE D   8      15.428  22.116  33.875  1.00  9.69      CC
ATOM   1767  CE1 PHE D   8      17.037  21.197  35.945  1.00 12.19      CC
ATOM   1768  CE2 PHE D   8      16.120  20.910  33.737  1.00 10.35      CC
ATOM   1769  CZ  PHE D   8      16.924  20.448  34.771  1.00  8.89      CC
ATOM   1770  C   PHE D   8      14.430  26.485  34.574  1.00 15.73      CC
ATOM   1771  O   PHE D   8      14.135  27.252  35.490  1.00 16.97      CC
ATOM   1772  N   HYP D   9      13.882  26.584  33.358  1.00 16.42      CC
ATOM   1773  CD  HYP D   9      14.495  26.153  32.089  1.00 18.36      CC
ATOM   1774  CA  HYP D   9      12.847  27.596  33.117  1.00 16.58      CC
ATOM   1775  CB  HYP D   9      12.654  27.534  31.609  1.00 17.03      CC
ATOM   1776  CG  HYP D   9      14.036  27.243  31.136  1.00 17.77      CC
ATOM   1777  C   HYP D   9      11.599  27.148  33.887  1.00 15.93      CC
ATOM   1778  O   HYP D   9      11.501  25.982  34.293  1.00 15.10      CC
ATOM   1779  OD  HYP D   9      14.095  26.856  29.776  1.00 21.73      CC
ATOM   1780  N   GLY D  10      10.653  28.055  34.094  1.00 13.77      CC
ATOM   1781  CA  GLY D  10       9.453  27.691  34.831  1.00 13.02      CC
ATOM   1782  C   GLY D  10       8.510  26.738  34.109  1.00 12.42      CC
ATOM   1783  O   GLY D  10       8.501  26.687  32.878  1.00 12.88      CC
ATOM   1784  N   GLU D  11       7.720  25.974  34.863  1.00 11.80      CC
ATOM   1785  CA  GLU D  11       6.754  25.051  34.260  1.00 12.74      CC
ATOM   1786  CB  GLU D  11       6.389  23.913  35.220  1.00 10.65      CC
ATOM   1787  CG  GLU D  11       7.500  22.914  35.476  1.00 10.47      CC
ATOM   1788  CD  GLU D  11       7.058  21.735  36.342  1.00  9.64      CC
ATOM   1789  OE1 GLU D  11       7.903  21.213  37.093  1.00 10.29      CC
ATOM   1790  OE2 GLU D  11       5.884  21.318  36.268  1.00  7.01      CC
ATOM   1791  C   GLU D  11       5.475  25.810  33.898  1.00 13.76      CC
ATOM   1792  O   GLU D  11       5.269  26.942  34.341  1.00 13.67      CC
ATOM   1793  N   ARG D  12       4.615  25.188  33.098  1.00 14.12      CC
ATOM   1794  CA  ARG D  12       3.356  25.828  32.709  1.00 14.59      CC
ATOM   1795  CB  ARG D  12       2.601  24.958  31.710  1.00 14.27      CC
ATOM   1796  CG  ARG D  12       3.451  24.479  30.569  1.00 16.49      CC
ATOM   1797  CD  ARG D  12       2.655  23.601  29.646  1.00 19.21      CC
ATOM   1798  NE  ARG D  12       3.525  22.833  28.762  1.00 22.96      CC
ATOM   1799  CZ  ARG D  12       3.096  21.868  27.963  1.00 21.61      CC
ATOM   1800  NH1 ARG D  12       1.806  21.563  27.940  1.00 22.39      CC
ATOM   1801  NH2 ARG D  12       3.954  21.199  27.207  1.00 23.45      CC
ATOM   1802  C   ARG D  12       2.508  25.990  33.959  1.00 13.43      CC
ATOM   1803  O   ARG D  12       2.670  25.239  34.916  1.00 13.31      CC
ATOM   1804  N   GLY D  13       1.602  26.961  33.948  1.00 12.98      CC
ATOM   1805  CA  GLY D  13       0.750  27.170  35.104  1.00 11.53      CC
ATOM   1806  C   GLY D  13      -0.199  26.006  35.345  1.00 11.89      CC
ATOM   1807  O   GLY D  13      -0.260  25.078  34.538  1.00  8.83      CC
ATOM   1808  N   PRO D  14      -0.947  26.016  36.464  1.00 12.32      CC
ATOM   1809  CD  PRO D  14      -1.005  27.064  37.497  1.00 11.59      CC
ATOM   1810  CA  PRO D  14      -1.890  24.933  36.764  1.00 12.45      CC
ATOM   1811  CB  PRO D  14      -2.364  25.275  38.174  1.00 13.04      CC
ATOM   1812  CG  PRO D  14      -2.319  26.762  38.187  1.00 11.93      CC
ATOM   1813  C   PRO D  14      -3.039  24.923  35.755  1.00 12.89      CC
ATOM   1814  O   PRO D  14      -3.289  25.928  35.082  1.00 12.39      CC
ATOM   1815  N   HYP D  15      -3.748  23.789  35.632  1.00 13.51      CC
ATOM   1816  CD  HYP D  15      -3.595  22.531  36.385  1.00 14.38      CC
ATOM   1817  CA  HYP D  15      -4.868  23.708  34.684  1.00 13.05      CC
ATOM   1818  CB  HYP D  15      -5.454  22.315  34.942  1.00 14.65      CC
ATOM   1819  CG  HYP D  15      -4.292  21.541  35.488  1.00 13.87      CC
ATOM   1820  C   HYP D  15      -5.877  24.811  34.990  1.00 12.80      CC
```

```
ATOM   1821  O   HYP D  15      -5.971  25.268  36.130  1.00 12.18      CC
ATOM   1822  OD  HYP D  15      -3.452  20.982  34.490  1.00 15.74      CC
ATOM   1823  N   GLY D  16      -6.623  25.237  33.973  1.00 13.68      CC
ATOM   1824  CA  GLY D  16      -7.619  26.277  34.165  1.00 13.35      CC
ATOM   1825  C   GLY D  16      -8.887  25.737  34.808  1.00 15.22      CC
ATOM   1826  O   GLY D  16      -9.015  24.529  35.002  1.00 14.14      CC
ATOM   1827  N   PRO D  17      -9.858  26.604  35.130  1.00 16.78      CC
ATOM   1828  CD  PRO D  17      -9.857  28.062  34.923  1.00 15.74      CC
ATOM   1829  CA  PRO D  17     -11.110  26.166  35.760  1.00 17.75      CC
ATOM   1830  CB  PRO D  17     -11.840  27.484  36.045  1.00 17.60      CC
ATOM   1831  CG  PRO D  17     -10.729  28.522  36.051  1.00 17.99      CC
ATOM   1832  C   PRO D  17     -11.945  25.237  34.884  1.00 18.61      CC
ATOM   1833  O   PRO D  17     -11.758  25.172  33.667  1.00 18.40      CC
ATOM   1834  N   HYP D  18     -12.876  24.489  35.498  1.00 19.66      CC
ATOM   1835  CD  HYP D  18     -13.157  24.363  36.939  1.00 19.82      CC
ATOM   1836  CA  HYP D  18     -13.720  23.580  34.715  1.00 19.63      CC
ATOM   1837  CB  HYP D  18     -14.608  22.924  35.778  1.00 21.13      CC
ATOM   1838  CG  HYP D  18     -13.760  22.991  37.010  1.00 20.32      CC
ATOM   1839  C   HYP D  18     -14.529  24.432  33.746  1.00 18.79      CC
ATOM   1840  O   HYP D  18     -14.809  25.592  34.033  1.00 18.95      CC
ATOM   1841  OD  HYP D  18     -12.787  21.962  37.083  1.00 23.21      CC
ATOM   1842  N   GLY D  19     -14.893  23.863  32.602  1.00 18.88      CC
ATOM   1843  CA  GLY D  19     -15.668  24.613  31.631  1.00 18.26      CC
ATOM   1844  C   GLY D  19     -17.104  24.824  32.078  1.00 18.68      CC
ATOM   1845  O   GLY D  19     -17.477  24.399  33.174  1.00 16.61      CC
ATOM   1846  N   PRO D  20     -17.938  25.502  31.265  1.00 19.16      CC
ATOM   1847  CD  PRO D  20     -17.561  26.245  30.055  1.00 19.89      CC
ATOM   1848  CA  PRO D  20     -19.342  25.752  31.604  1.00 20.26      CC
ATOM   1849  CB  PRO D  20     -19.732  26.886  30.660  1.00 20.83      CC
ATOM   1850  CG  PRO D  20     -18.412  27.463  30.179  1.00 20.62      CC
ATOM   1851  C   PRO D  20     -20.162  24.491  31.300  1.00 21.06      CC
ATOM   1852  O   PRO D  20     -19.697  23.616  30.577  1.00 20.72      CC
ATOM   1853  N   HYP D  21     -21.378  24.377  31.859  1.00 21.33      CC
ATOM   1854  CD  HYP D  21     -21.927  25.146  32.992  1.00 21.67      CC
ATOM   1855  CA  HYP D  21     -22.215  23.189  31.590  1.00 21.74      CC
ATOM   1856  CB  HYP D  21     -23.468  23.451  32.440  1.00 22.13      CC
ATOM   1857  CG  HYP D  21     -22.878  24.155  33.631  1.00 21.33      CC
ATOM   1858  C   HYP D  21     -22.551  23.036  30.094  1.00 21.48      CC
ATOM   1859  O   HYP D  21     -22.726  24.026  29.378  1.00 22.03      CC
ATOM   1860  OD  HYP D  21     -22.228  23.265  34.516  1.00 23.21      CC
ATOM   1861  N   NHH D  22     -22.657  21.806  29.613  1.00 20.91      CC
TER
ATOM   1862  O   HOH E 401      16.330  14.217  61.265  1.00  7.27      W
ATOM   1863  O   HOH E 402      19.752  18.951  37.584  1.00 15.74      W
ATOM   1864  O   HOH E 403       2.016  10.266  32.905  1.00 23.77      W
ATOM   1865  O   HOH E 404       4.266  11.763  34.068  1.00  9.44      W
ATOM   1866  O   HOH E 405      10.519  11.274  32.006  1.00 21.51      W
ATOM   1867  O   HOH E 406       1.504  12.266  29.042  1.00 21.77      W
ATOM   1868  O   HOH E 407      20.908  16.308  36.153  1.00 17.64      W
ATOM   1869  O   HOH E 408      17.091  20.929  39.613  1.00 12.14      W
ATOM   1870  O   HOH E 409       8.326  -0.946  34.265  1.00 26.84      W
ATOM   1871  O   HOH E 410      10.585  22.363  46.723  1.00 11.87      W
ATOM   1872  O   HOH E 411      25.378  10.794  55.016  1.00 24.26      W
ATOM   1873  O   HOH E 412      20.406  16.105  51.398  1.00 11.61      W
ATOM   1874  O   HOH E 413      16.878  25.139  38.620  1.00 14.37      W
ATOM   1875  O   HOH E 414      -0.842  16.913  58.285  1.00 16.87      W
```

ATOM	1876	O	HOH E 415	10.411	24.807	49.914	1.00	52.97		W
ATOM	1877	O	HOH E 416	13.368	22.460	47.864	1.00	18.07		W
ATOM	1878	O	HOH E 417	13.150	11.289	62.240	1.00	47.74		W
ATOM	1879	O	HOH E 418	1.303	-6.147	47.976	1.00	16.49		W
ATOM	1880	O	HOH E 419	8.599	13.854	30.673	1.00	18.89		W
ATOM	1881	O	HOH E 420	10.232	-2.382	37.701	1.00	14.49		W
ATOM	1882	O	HOH E 421	-3.601	4.030	52.968	1.00	15.10		W
ATOM	1883	O	HOH E 422	5.410	-7.210	42.591	1.00	21.64		W
ATOM	1884	O	HOH E 423	3.279	-9.212	44.213	1.00	29.74		W
ATOM	1885	O	HOH E 424	-16.951	19.401	35.082	1.00	34.19		W
ATOM	1886	O	HOH E 425	-1.522	17.595	32.378	1.00	24.97		W
ATOM	1887	O	HOH E 426	8.884	13.210	58.870	1.00	25.98		W
ATOM	1888	O	HOH E 427	11.250	14.511	57.508	1.00	10.37		W
ATOM	1889	O	HOH E 428	-2.929	10.128	32.874	1.00	37.15		W
ATOM	1890	O	HOH E 429	-2.009	12.948	33.369	1.00	17.55		W
ATOM	1891	O	HOH E 430	-5.571	16.309	35.097	1.00	32.24		W
ATOM	1892	O	HOH E 431	-4.389	33.187	33.783	1.00	18.95		W
ATOM	1893	O	HOH E 432	15.969	10.887	53.476	1.00	32.71		W
ATOM	1894	O	HOH E 433	14.711	22.985	29.797	1.00	54.65		W
ATOM	1895	O	HOH E 434	4.779	-4.755	31.380	1.00	28.71		W
ATOM	1896	O	HOH E 435	-5.058	10.030	50.214	1.00	28.66		W
ATOM	1897	O	HOH E 436	-16.040	29.691	30.628	1.00	30.05		W
ATOM	1898	O	HOH E 437	-7.659	20.017	35.921	1.00	29.62		W
ATOM	1899	O	HOH E 438	7.624	5.929	62.247	1.00	18.95		W
ATOM	1900	O	HOH E 439	5.101	33.897	32.954	1.00	15.88		W
ATOM	1901	O	HOH E 440	20.979	6.175	33.371	1.00	32.22		W
ATOM	1902	O	HOH E 441	-6.393	32.120	30.613	1.00	29.97		W
ATOM	1903	O	HOH E 442	23.467	19.968	39.168	1.00	40.58		W
ATOM	1904	O	HOH E 443	15.123	6.339	30.675	1.00	22.32		W
ATOM	1905	O	HOH E 444	-2.185	1.475	51.922	1.00	30.14		W
ATOM	1906	O	HOH E 445	16.868	-11.187	38.112	1.00	33.83		W
ATOM	1907	O	HOH E 446	9.709	29.020	43.378	1.00	47.17		W
ATOM	1908	O	HOH E 447	9.022	20.434	54.535	1.00	39.15		W
ATOM	1909	O	HOH E 448	18.161	0.376	56.588	1.00	41.53		W
ATOM	1910	O	HOH E 449	1.292	37.093	34.663	1.00	39.13		W
ATOM	1911	O	HOH E 450	-5.218	28.339	39.373	1.00	20.28		W
ATOM	1912	O	HOH E 451	-18.990	23.798	35.404	1.00	22.93		W
ATOM	1913	O	HOH E 452	15.022	35.511	35.405	1.00	34.37		W
ATOM	1914	O	HOH E 453	11.191	32.962	36.498	1.00	14.69		W
ATOM	1915	O	HOH E 454	15.768	-4.887	52.120	1.00	22.65		W
ATOM	1916	O	HOH E 455	1.460	-6.101	37.435	1.00	20.27		W
ATOM	1917	O	HOH E 456	2.850	-3.540	37.375	1.00	21.11		W
ATOM	1918	O	HOH E 457	-0.387	-3.197	40.345	1.00	22.30		W
ATOM	1919	O	HOH E 458	17.628	33.001	33.070	1.00	28.12		W
ATOM	1920	O	HOH E 459	20.718	33.705	32.843	1.00	47.02		W
ATOM	1921	O	HOH E 460	12.058	-13.328	39.611	1.00	28.23		W
ATOM	1922	O	HOH E 461	19.085	-13.047	45.158	1.00	36.96		W
ATOM	1923	O	HOH E 462	25.263	12.268	35.569	1.00	33.88		W
ATOM	1924	O	HOH E 463	1.677	-5.057	32.759	1.00	35.05		W
ATOM	1925	O	HOH E 464	13.210	-5.412	32.844	1.00	19.95		W
ATOM	1926	O	HOH E 465	20.199	2.558	34.558	1.00	23.92		W
ATOM	1927	O	HOH E 466	10.903	11.186	29.019	1.00	22.99		W
ATOM	1928	O	HOH E 467	12.411	31.695	40.333	1.00	18.47		W
ATOM	1929	O	HOH E 468	18.494	31.420	41.330	1.00	36.00		W
ATOM	1930	O	HOH E 469	0.713	30.644	38.709	1.00	32.15		W
ATOM	1931	O	HOH E 470	4.495	-7.749	54.370	1.00	27.53		W

ATOM	1932	O	HOH E 471	4.455	16.672	59.168	1.00	33.94	W
ATOM	1933	O	HOH E 472	-7.327	18.714	30.650	1.00	75.20	W
ATOM	1934	O	HOH E 473	-15.390	28.107	33.235	1.00	23.19	W
ATOM	1935	O	HOH E 474	-25.202	16.177	24.609	1.00	30.95	W
ATOM	1936	O	HOH E 475	7.128	18.700	40.698	1.00	16.55	W
ATOM	1937	O	HOH E 476	23.267	16.273	48.985	1.00	56.29	W
ATOM	1938	O	HOH E 477	28.423	-0.449	48.099	1.00	28.46	W
ATOM	1939	O	HOH E 478	18.290	5.977	30.269	1.00	35.16	W
ATOM	1940	O	HOH E 479	-2.932	19.947	46.633	1.00	37.58	W
ATOM	1941	O	HOH E 480	-6.995	14.103	33.192	1.00	41.98	W
ATOM	1942	O	HOH E 481	19.155	28.681	30.733	1.00	41.30	W
ATOM	1943	O	HOH E 482	8.752	19.818	28.348	1.00	18.61	W
ATOM	1944	O	HOH E 483	13.768	-10.940	38.730	1.00	25.60	W
ATOM	1945	O	HOH E 484	-9.232	12.028	47.636	1.00	29.15	W
ATOM	1946	O	HOH E 485	25.768	-2.672	34.238	1.00	19.91	W
ATOM	1947	O	HOH E 486	-9.793	8.985	29.027	1.00	47.04	W
ATOM	1948	O	HOH E 487	36.629	34.002	46.802	1.00	36.63	W
ATOM	1949	O	HOH E 488	-10.031	3.831	41.340	1.00	23.32	W
ATOM	1950	O	HOH E 489	3.698	-8.671	31.566	1.00	26.69	W
ATOM	1951	O	HOH E 490	16.860	-15.407	49.734	1.00	42.23	W
ATOM	1952	O	HOH E 491	-1.973	-11.244	43.332	1.00	54.06	W
ATOM	1953	O	HOH E 492	2.252	-3.277	56.623	1.00	59.17	W
ATOM	1954	O	HOH E 493	-0.813	20.662	43.718	1.00	29.10	W
ATOM	1955	O	HOH E 494	27.179	32.232	34.060	1.00	33.41	W
ATOM	1956	O	HOH E 495	9.702	16.259	28.490	1.00	30.80	W
ATOM	1957	O	HOH E 496	-5.273	5.984	51.412	1.00	26.74	W
ATOM	1958	O	HOH E 497	12.811	20.705	25.466	1.00	36.98	W
ATOM	1959	O	HOH E 498	4.397	-2.916	59.475	1.00	45.37	W
ATOM	1960	O	HOH E 499	21.810	20.049	42.888	1.00	25.48	W
ATOM	1961	O	HOH E 500	29.335	-5.682	39.527	1.00	29.98	W
ATOM	1962	O	HOH E 501	-4.035	1.559	59.722	1.00	48.77	W
ATOM	1963	O	HOH E 502	24.853	-4.028	51.970	1.00	29.73	W
ATOM	1964	O	HOH E 503	8.735	12.981	27.657	1.00	25.99	W
ATOM	1965	O	HOH E 504	4.608	5.432	66.221	1.00	39.32	W
ATOM	1966	O	HOH E 505	8.157	26.632	37.716	1.00	19.09	W
ATOM	1967	O	HOH E 506	19.925	21.667	40.974	1.00	30.96	W
ATOM	1968	O	HOH E 507	21.123	21.624	38.019	1.00	57.54	W
ATOM	1969	O	HOH E 508	19.670	4.586	54.357	1.00	18.45	W
ATOM	1970	O	HOH E 509	16.405	2.164	52.694	1.00	15.67	W
ATOM	1971	O	HOH E 510	17.181	3.240	55.387	1.00	20.43	W
ATOM	1972	O	HOH E 511	10.379	22.476	43.820	1.00	10.33	W
ATOM	1973	O	HOH E 512	-5.658	18.433	37.515	1.00	9.41	W
ATOM	1974	O	HOH E 513	-0.352	11.410	31.231	1.00	22.75	W
ATOM	1975	O	HOH E 514	-1.032	-6.393	39.369	1.00	71.81	W
ATOM	1976	O	HOH E 515	12.801	14.283	61.993	1.00	43.75	W
ATOM	1977	O	HOH E 516	0.335	-7.160	34.633	1.00	43.12	W
ATOM	1978	O	HOH E 517	18.740	9.195	34.517	1.00	21.42	W
ATOM	1979	O	HOH E 518	21.092	26.747	46.523	1.00	37.98	W
ATOM	1980	O	HOH E 519	-0.634	-5.353	30.779	1.00	31.44	W
ATOM	1981	O	HOH E 520	9.702	29.614	29.819	1.00	39.63	W
ATOM	1982	O	HOH E 521	2.103	31.457	25.374	1.00	60.68	W
ATOM	1983	O	HOH E 522	21.839	23.414	46.265	1.00	27.45	W
ATOM	1984	O	HOH E 523	-1.829	-6.665	43.612	1.00	38.69	W
ATOM	1985	O	HOH E 524	-16.318	15.309	29.036	1.00	29.84	W
ATOM	1986	O	HOH E 525	12.381	9.143	26.968	1.00	35.75	W
ATOM	1987	O	HOH E 526	-9.464	13.244	43.157	1.00	15.14	W

ATOM	1988	O	HOH E 527	1.957	19.483	58.941	1.00	44.43	W
ATOM	1989	O	HOH E 528	-7.641	5.258	33.722	1.00	42.72	W
ATOM	1990	O	HOH E 529	9.446	17.350	65.141	1.00	58.61	W
ATOM	1991	O	HOH E 530	26.874	39.005	45.593	1.00	38.89	W
ATOM	1992	O	HOH E 531	21.700	9.818	32.431	1.00	29.79	W
ATOM	1993	O	HOH E 532	19.909	37.845	37.897	1.00	45.65	W
ATOM	1994	O	HOH E 533	-4.483	18.944	32.657	1.00	29.09	W
ATOM	1995	O	HOH E 534	5.879	18.842	61.111	1.00	25.87	W
ATOM	1996	O	HOH E 535	14.645	-14.638	53.958	1.00	34.91	W
ATOM	1997	O	HOH E 536	10.758	23.693	29.607	1.00	39.53	W
ATOM	1998	O	HOH E 537	14.338	29.236	52.072	1.00	23.79	W
ATOM	1999	O	HOH E 538	-1.741	9.523	54.031	1.00	15.67	W
ATOM	2000	O	HOH E 539	37.974	28.457	47.538	1.00	37.53	W
ATOM	2001	O	HOH E 540	-4.043	22.878	40.941	1.00	24.51	W
ATOM	2002	O	HOH E 541	-10.067	3.093	33.051	1.00	39.04	W
ATOM	2003	O	HOH E 542	23.692	16.947	40.249	1.00	37.69	W
ATOM	2004	O	HOH E 543	-14.538	18.262	36.711	1.00	25.98	W
ATOM	2005	O	HOH E 544	-21.782	25.567	27.128	1.00	22.21	W
ATOM	2006	O	HOH E 545	-6.512	24.664	43.761	1.00	24.02	W
ATOM	2007	O	HOH E 546	0.663	-12.626	51.997	1.00	21.29	W
ATOM	2008	O	HOH E 547	5.183	-4.422	55.353	1.00	28.59	W
ATOM	2009	O	HOH E 548	15.427	-11.562	53.600	1.00	41.82	W
ATOM	2010	O	HOH E 549	-6.105	0.971	34.469	1.00	33.69	W
ATOM	2011	O	HOH E 550	24.009	14.010	45.618	1.00	31.33	W
ATOM	2012	O	HOH E 551	28.845	1.189	53.843	1.00	25.92	W
ATOM	2013	O	HOH E 552	22.693	-2.757	30.748	1.00	39.50	W
ATOM	2014	O	HOH E 553	14.366	8.993	63.904	1.00	27.99	W
ATOM	2015	O	HOH E 554	-2.851	7.676	50.104	1.00	6.24	W
ATOM	2016	O	HOH E 555	-21.496	18.740	25.299	1.00	37.92	W
ATOM	2017	O	HOH E 556	-4.586	-0.965	54.920	1.00	32.72	W
ATOM	2018	O	HOH E 557	28.684	7.487	39.407	1.00	38.90	W
ATOM	2019	O	HOH E 558	-4.261	27.809	42.326	1.00	38.34	W
ATOM	2020	O	HOH E 559	27.593	12.602	39.403	1.00	33.36	W
ATOM	2021	O	HOH E 560	5.408	21.728	39.073	1.00	18.41	W
ATOM	2022	O	HOH E 561	4.934	33.417	35.974	1.00	41.20	W
ATOM	2023	O	HOH E 562	20.940	-9.117	33.600	1.00	37.49	W
ATOM	2024	O	HOH E 563	25.023	4.235	34.909	1.00	32.12	W
ATOM	2025	O	HOH E 564	-7.915	31.142	34.213	1.00	20.84	W
ATOM	2026	O	HOH E 565	25.443	21.564	41.029	1.00	29.81	W
ATOM	2027	O	HOH E 566	7.224	3.183	57.981	1.00	18.29	W
ATOM	2028	O	HOH E 567	-11.011	17.891	38.676	1.00	54.99	W
ATOM	2029	O	HOH E 568	27.552	-6.668	34.568	1.00	57.12	W
ATOM	2030	O	HOH E 569	-9.431	19.864	28.498	1.00	33.60	W
ATOM	2031	O	HOH E 570	-9.953	33.734	35.439	1.00	38.58	W
ATOM	2032	O	HOH E 571	15.884	-3.180	55.349	1.00	42.47	W
ATOM	2033	O	HOH E 572	9.077	20.453	25.079	1.00	34.23	W
ATOM	2034	O	HOH E 573	27.196	8.842	33.494	1.00	28.68	W
ATOM	2035	O	HOH E 574	3.622	-14.068	39.777	1.00	40.01	W
ATOM	2036	O	HOH E 575	22.780	-6.705	48.821	1.00	35.65	W
ATOM	2037	O	HOH E 576	20.461	14.459	53.991	1.00	7.42	W
ATOM	2038	O	HOH E 577	27.952	24.030	44.546	1.00	49.20	W
ATOM	2039	O	HOH E 578	2.048	26.398	43.059	1.00	38.93	W
ATOM	2040	O	HOH E 579	18.772	13.735	50.322	1.00	14.30	W
ATOM	2041	O	HOH E 580	28.890	4.103	47.890	1.00	39.36	W
ATOM	2042	O	HOH E 581	16.438	0.081	60.966	1.00	45.15	W
ATOM	2043	O	HOH E 582	6.734	26.793	26.473	1.00	55.90	W

ATOM	2044	O	HOH E 583	1.207	4.137	65.627	1.00	45.41	W
ATOM	2045	O	HOH E 584	7.326	-9.176	55.828	1.00	55.37	W
ATOM	2046	O	HOH E 585	-5.971	-6.427	38.603	1.00	31.68	W
ATOM	2047	O	HOH E 586	3.834	-8.745	40.456	1.00	20.37	W
ATOM	2048	O	HOH E 587	18.895	-15.206	53.910	1.00	36.75	W
ATOM	2049	O	HOH E 588	10.278	12.294	61.398	1.00	49.20	W
ATOM	2050	O	HOH E 589	23.956	15.507	34.852	1.00	41.12	W
ATOM	2051	O	HOH E 590	-0.393	16.534	29.704	1.00	50.39	W
ATOM	2052	O	HOH E 591	28.619	-2.738	54.840	1.00	60.38	W
ATOM	2053	O	HOH E 592	16.294	-17.370	59.916	1.00	37.59	W
ATOM	2054	O	HOH E 593	26.970	17.196	40.746	1.00	51.31	W
ATOM	2055	O	HOH E 594	19.730	-17.598	48.544	1.00	40.50	W
ATOM	2056	O	HOH E 595	1.326	0.954	59.482	1.00	34.91	W
ATOM	2057	O	HOH E 596	-9.799	9.892	37.138	1.00	33.55	W
ATOM	2058	O	HOH E 597	-0.061	-9.253	45.965	1.00	50.81	W
ATOM	2059	O	HOH E 598	-9.383	16.434	31.738	1.00	80.11	W
ATOM	2060	O	HOH E 599	28.769	8.640	42.670	1.00	43.27	W
ATOM	2061	O	HOH E 600	-0.063	-14.933	49.352	1.00	49.59	W
ATOM	2062	O	HOH E 601	-3.092	19.360	39.749	1.00	10.48	W
ATOM	2063	O	HOH E 602	2.098	30.090	44.138	1.00	33.04	W
ATOM	2064	O	HOH E 603	16.517	-5.223	41.821	1.00	13.16	W
ATOM	2065	O	HOH E 604	13.725	-15.908	43.046	1.00	50.39	W
ATOM	2066	O	HOH E 605	-8.398	-0.815	36.648	1.00	44.78	W
ATOM	2067	O	HOH E 606	-11.723	16.827	35.869	1.00	45.21	W
ATOM	2068	O	HOH E 607	21.277	-5.651	56.343	1.00	29.34	W
ATOM	2069	O	HOH E 608	0.385	28.090	25.264	1.00	30.39	W
ATOM	2070	O	HOH E 609	22.972	36.785	37.710	1.00	61.85	W
ATOM	2071	O	HOH E 610	-22.932	23.819	37.010	1.00	35.16	W
ATOM	2072	O	HOH E 611	-0.053	32.476	43.573	1.00	47.38	W
ATOM	2073	O	HOH E 612	16.349	-4.295	32.442	1.00	11.94	W
ATOM	2074	O	HOH E 613	8.944	17.294	55.291	1.00	38.30	W
ATOM	2075	O	HOH E 614	-12.696	5.454	42.347	1.00	24.01	W
ATOM	2076	O	HOH E 615	9.177	8.214	28.044	1.00	14.97	W
ATOM	2077	O	HOH E 616	0.445	33.900	38.846	1.00	49.81	W
ATOM	2078	O	HOH E 617	21.274	-2.650	56.811	1.00	51.42	W
ATOM	2079	O	HOH E 618	-10.014	10.985	40.675	1.00	19.46	W
ATOM	2080	O	HOH E 619	-0.454	23.829	44.924	1.00	45.60	W
ATOM	2081	O	HOH E 620	11.214	19.178	21.651	1.00	43.14	W
ATOM	2082	O	HOH E 621	0.405	-9.345	49.102	1.00	29.74	W
ATOM	2083	O	HOH E 622	12.410	20.925	30.282	1.00	32.22	W
ATOM	2084	O	HOH E 623	1.346	-7.579	51.489	1.00	37.32	W
ATOM	2085	O	HOH E 624	0.952	-1.848	62.790	1.00	40.55	W
ATOM	2086	O	HOH E 625	25.065	35.727	35.689	1.00	49.74	W
ATOM	2087	O	HOH E 626	-0.370	-8.630	31.015	1.00	29.03	W
ATOM	2088	O	HOH E 627	-16.728	15.876	25.532	1.00	30.88	W
ATOM	2089	O	HOH E 628	6.938	-5.411	53.020	1.00	42.93	W
ATOM	2090	O	HOH E 629	24.380	1.854	32.909	1.00	47.21	W
ATOM	2091	O	HOH E 630	-8.097	-0.898	58.999	1.00	26.17	W
ATOM	2092	O	HOH E 631	6.349	26.620	30.559	1.00	19.66	W
ATOM	2093	O	HOH E 632	-2.843	-4.402	37.498	1.00	36.21	W
ATOM	2094	O	HOH E 633	-11.910	13.215	48.308	1.00	38.00	W
ATOM	2095	O	HOH E 634	-3.324	-7.892	37.394	1.00	38.68	W
ATOM	2096	O	HOH E 635	24.398	-13.158	48.927	1.00	43.76	W
ATOM	2097	O	HOH E 636	-8.198	-5.459	47.003	1.00	27.11	W
ATOM	2098	O	HOH E 637	-8.309	2.465	36.126	1.00	41.61	W
ATOM	2099	O	HOH E 638	11.803	20.581	62.626	1.00	35.46	W

ATOM	2100	O	HOH E 639	10.945	19.084	58.586	1.00	45.01	W
ATOM	2101	O	HOH E 640	24.849	29.419	47.628	1.00	43.17	W
ATOM	2102	O	HOH E 641	29.935	-2.937	50.468	1.00	46.17	W
ATOM	2103	O	HOH E 642	-13.168	15.458	33.377	1.00	44.29	W
ATOM	2104	O	HOH E 643	30.171	-8.396	50.663	1.00	44.09	W
ATOM	2105	O	HOH E 644	-3.800	-10.918	49.026	1.00	42.03	W
ATOM	2106	O	HOH E 645	-11.802	13.503	31.227	1.00	32.17	W
ATOM	2107	O	HOH E 646	25.724	15.828	32.256	1.00	47.08	W
ATOM	2108	O	HOH E 647	23.197	36.930	41.760	1.00	59.31	W
ATOM	2109	O	HOH E 648	6.297	13.476	62.219	1.00	20.21	W
ATOM	2110	O	HOH E 649	26.923	39.279	48.907	1.00	38.82	W
ATOM	2111	O	HOH E 650	-11.912	28.753	27.748	1.00	15.52	W
ATOM	2112	O	HOH E 651	-1.841	0.730	55.015	1.00	34.19	W
ATOM	2113	O	HOH E 652	27.087	19.363	43.124	1.00	35.99	W
ATOM	2114	O	HOH E 653	-5.759	32.720	51.478	1.00	42.93	W
ATOM	2115	O	HOH E 654	2.519	-7.426	58.675	1.00	44.06	W
ATOM	2116	O	HOH E 655	19.199	36.052	31.423	1.00	50.09	W
ATOM	2117	O	HOH E 656	36.482	33.963	37.970	1.00	29.85	W
ATOM	2118	O	HOH E 657	17.605	38.239	35.191	1.00	49.64	W
ATOM	2119	O	HOH E 658	-6.132	-1.762	40.679	1.00	58.90	W
ATOM	2120	O	HOH E 659	16.738	-12.983	56.218	1.00	26.39	W
ATOM	2121	O	HOH E 660	30.120	2.212	50.795	1.00	47.95	W
ATOM	2122	O	HOH E 661	-2.330	32.018	54.211	1.00	22.05	W
ATOM	2123	O	HOH E 662	26.040	10.878	43.103	1.00	58.31	W
ATOM	2124	O	HOH E 663	12.297	13.980	28.533	1.00	28.23	W
ATOM	2125	O	HOH E 664	29.821	12.619	35.702	1.00	36.51	W
ATOM	2126	O	HOH E 665	-4.617	-1.126	50.876	1.00	38.50	W
ATOM	2127	O	HOH E 666	24.545	-0.669	55.100	1.00	32.21	W
ATOM	2128	O	HOH E 667	-7.088	31.748	54.539	1.00	38.30	W
ATOM	2129	O	HOH E 668	28.885	15.172	42.351	1.00	38.33	W
ATOM	2130	O	HOH E 669	-10.569	21.693	38.518	1.00	38.74	W
ATOM	2131	O	HOH E 670	21.244	5.913	29.116	1.00	61.57	W
ATOM	2132	O	HOH E 671	-5.925	23.682	38.495	1.00	35.75	W
ATOM	2133	O	HOH E 672	-5.893	25.939	47.728	1.00	31.91	W
ATOM	2134	O	HOH E 673	4.714	-10.124	59.049	1.00	47.84	W
ATOM	2135	O	HOH E 674	-7.727	-4.136	55.451	1.00	24.28	W
ATOM	2136	O	HOH E 675	8.051	-12.031	31.037	1.00	26.07	W
ATOM	2137	O	HOH E 676	6.482	12.323	23.254	1.00	41.15	W
ATOM	2138	O	HOH E 677	28.692	38.404	43.002	1.00	53.47	W
ATOM	2139	O	HOH E 678	8.274	3.989	68.327	1.00	29.04	W
ATOM	2140	O	HOH E 679	14.925	-15.917	62.867	1.00	30.26	W
ATOM	2141	O	HOH E 680	25.612	12.902	48.272	1.00	68.00	W
ATOM	2142	O	HOH E 681	12.405	4.058	68.632	1.00	29.34	W
ATOM	2143	O	HOH E 682	16.645	26.144	28.767	1.00	37.16	W
ATOM	2144	O	HOH E 683	4.557	0.245	60.083	1.00	46.50	W
ATOM	2145	O	HOH E 684	23.005	-9.610	47.006	1.00	39.61	W
ATOM	2146	O	HOH E 685	-15.268	27.535	28.052	1.00	56.53	W
ATOM	2147	O	HOH E 686	-3.271	32.616	30.463	1.00	32.99	W
ATOM	2148	O	HOH E 687	-1.210	-0.738	58.568	1.00	67.47	W
ATOM	2149	O	HOH E 688	27.788	35.525	47.975	1.00	40.99	W
ATOM	2150	O	HOH E 689	2.086	34.462	35.942	1.00	27.35	W
ATOM	2151	O	HOH E 690	10.069	2.633	70.673	1.00	49.43	W
ATOM	2152	O	HOH E 691	21.297	-14.655	49.191	1.00	49.35	W
ATOM	2153	O	HOH E 692	19.982	-16.815	59.582	1.00	56.16	W
ATOM	2154	O	HOH E 693	20.800	35.579	40.253	1.00	48.20	W
ATOM	2155	O	HOH E 694	24.030	6.818	32.263	1.00	50.91	W

ATOM	2156	O	HOH E 695	-1.111	27.060	46.541	1.00	17.67		W
ATOM	2157	O	HOH E 696	-27.078	18.341	26.678	1.00	55.01		W
ATOM	2158	O	HOH E 697	-10.231	0.457	56.323	1.00	33.31		W
ATOM	2159	O	HOH E 698	4.275	-2.353	63.270	1.00	40.77		W
ATOM	2160	O	HOH E 699	28.449	24.425	47.948	1.00	32.19		W
ATOM	2161	O	HOH E 700	30.889	38.367	39.277	1.00	54.24		W
ATOM	2162	O	HOH E 701	6.516	33.704	54.312	1.00	24.50		W
ATOM	2163	O	HOH E 702	9.479	32.909	53.611	1.00	53.53		W
ATOM	2164	O	HOH E 703	9.352	29.832	54.842	1.00	34.81		W
ATOM	2165	O	HOH E 704	26.759	36.138	40.043	1.00	30.98		W
ATOM	2166	O	HOH E 705	29.458	-6.695	53.369	1.00	47.75		W
ATOM	2167	O	HOH E 706	5.033	-10.973	29.828	1.00	27.71		W
ATOM	2168	O	HOH E 707	27.793	-9.749	35.681	1.00	31.20		W
ATOM	2169	O	HOH E 708	31.071	-1.537	53.144	1.00	32.97		W
ATOM	2170	O	HOH E 709	-3.807	22.472	44.590	1.00	46.35		W
ATOM	2171	O	HOH E 710	-4.795	-7.128	44.799	1.00	28.48		W
ATOM	2172	O	HOH E 711	-12.586	1.440	45.045	1.00	36.39		W
ATOM	2173	O	HOH E 712	-5.260	3.802	61.612	1.00	40.65		W
ATOM	2174	O	HOH E 713	29.964	1.189	35.812	1.00	34.49		W
ATOM	2175	O	HOH E 714	-2.343	-12.035	40.222	1.00	69.00		W
ATOM	2176	O	HOH E 715	9.302	23.483	53.331	1.00	44.74		W
ATOM	2177	O	HOH E 716	-2.242	-2.626	62.126	1.00	38.70		W
ATOM	2178	O	HOH E 717	-7.275	0.894	52.443	1.00	54.44		W
ATOM	2179	O	HOH E 718	-8.110	15.858	43.753	1.00	42.70		W
ATOM	2180	O	HOH E 719	26.788	-8.036	52.120	1.00	40.32		W
ATOM	2181	O	HOH E 720	6.407	3.434	64.438	1.00	28.31		W
ATOM	2182	O	HOH E 721	-5.768	15.496	29.504	1.00	39.40		W
ATOM	2183	O	HOH E 722	31.860	30.480	48.051	1.00	35.91		W
ATOM	2184	O	HOH E 723	-2.018	-11.813	46.456	1.00	40.13		W
ATOM	2185	O	HOH E 724	-14.067	13.952	45.904	1.00	30.17		W
ATOM	2186	O	HOH E 725	11.597	22.036	22.756	1.00	43.20		W
ATOM	2187	O	HOH E 726	12.253	25.948	27.576	1.00	42.36		W
ATOM	2188	O	HOH E 727	0.693	-4.936	60.187	1.00	55.60		W
ATOM	2189	O	HOH E 728	3.595	14.524	25.741	1.00	30.29		W
ATOM	2190	O	HOH E 729	29.954	37.854	47.035	1.00	52.60		W
ATOM	2191	O	HOH E 730	-2.366	30.916	41.868	1.00	55.38		W
ATOM	2192	O	HOH E 731	8.713	-11.641	36.683	1.00	30.73		W
ATOM	2193	O	HOH E 732	0.761	-5.195	53.384	1.00	38.64		W
ATOM	2194	O	HOH E 733	31.365	26.739	47.933	1.00	31.61		W
ATOM	2195	O	HOH E 734	7.345	16.504	26.173	1.00	64.82		W
ATOM	2196	O	HOH E 735	10.677	0.163	68.748	1.00	36.34		W
ATOM	2197	O	HOH E 736	27.161	35.880	32.022	1.00	33.61		W
ATOM	2198	O	HOH E 737	-13.094	10.266	30.707	1.00	43.14		W
ATOM	2199	O	HOH E 738	-10.853	17.032	27.531	1.00	38.09		W
ATOM	2200	O	HOH E 739	3.458	16.325	42.437	1.00	7.40		W
ATOM	2201	O	HOH E 740	1.544	-12.771	41.970	1.00	43.59		W
ATOM	2202	O	HOH E 741	-1.559	2.106	29.784	1.00	31.14		W
ATOM	2203	O	HOH E 742	12.165	-12.601	53.138	1.00	28.68		W
ATOM	2204	O	HOH E 743	-7.457	9.069	33.302	1.00	55.50		W
ATOM	2205	O	HOH E 744	38.921	31.695	46.548	1.00	26.37		W
ATOM	2206	O	HOH E 745	10.857	-10.683	32.696	1.00	39.32		W
ATOM	2207	O	HOH E 746	22.495	18.359	51.539	1.00	63.86		W
ATOM	2208	O	HOH E 747	-2.309	34.601	37.405	1.00	44.56		W
ATOM	2209	O	HOH E 748	27.912	17.187	45.245	1.00	46.22		W
ATOM	2210	O	HOH E 749	-5.769	11.268	31.499	1.00	57.12		W
ATOM	2211	O	HOH E 750	-9.792	14.584	34.747	1.00	49.85		W

```
ATOM   2212  O   HOH E 751     -11.874  -1.486  58.793  1.00 44.85      W
ATOM   2213  O   HOH E 752      27.694  25.282  40.488  1.00 33.06      W
ATOM   2214  O   HOH E 753      -4.429   3.543  33.226  1.00 55.03      W
ATOM   2215  O   HOH E 754       9.486  26.613  30.244  1.00 28.82      W
ATOM   2216  O   HOH E 755      16.245  21.348  27.760  1.00 49.05      W
ATOM   2217  O   HOH E 756       5.957 -12.920  38.184  1.00 55.64      W
ATOM   2218  O   HOH E 757      -1.395  -3.051  52.384  1.00 36.76      W
ATOM   2219  O   HOH E 758     -23.397  28.050  27.312  1.00 49.99      W
ATOM   2220  O   HOH E 759      -3.913  17.130  47.667  1.00 40.93      W
ATOM   2221  O   HOH E 760       8.477  -3.858  56.162  1.00 32.91      W
ATOM   2222  O   HOH E 762      26.500  -4.882  49.324  1.00 61.66      W
ATOM   2223  O   HOH E 763       3.962  17.618  26.722  1.00 44.99      W
ATOM   2224  O   HOH E 764      -7.442  30.127  37.158  1.00 47.35      W
ATOM   2225  O   HOH E 765      -9.170   1.976  59.674  1.00 40.00      W
ATOM   2226  O   HOH E 766       1.556  -9.249  54.896  1.00 46.10      W
ATOM   2227  O   HOH E 767      23.553  11.164  30.150  1.00 57.11      W
ATOM   2228  O   HOH E 768      -6.304  -9.029  42.535  1.00 34.59      W
ATOM   2229  O   HOH E 769      12.201  26.847  52.874  1.00 44.51      W
ATOM   2230  O   HOH E 770       8.167  36.689  53.755  1.00 42.84      W
ATOM   2231  O   HOH E 771       7.844  25.653  40.709  1.00 11.73      W
ATOM   2232  O   HOH E 772      10.893  -0.048  52.560  1.00 29.20      W
ATOM   2233  O   HOH E 773       5.664   0.278  57.220  1.00 21.93      W
ATOM   2234  O   HOH E 774       5.263  27.600  45.159  1.00 20.60      W
ATOM   2235  O   HOH E 775      17.170  -3.453  39.193  1.00 18.37      W
ATOM   2236  O   HOH E 776      -2.126  -9.071  34.451  1.00 27.96      W
ATOM   2237  O   HOH E 777      26.372  -0.053  36.568  1.00 32.03      W
ATOM   2238  O   HOH E 778      11.643  -4.518  55.330  1.00 27.32      W
ATOM   2239  O   HOH E 779      -7.701  28.135  54.948  1.00 37.66      W
ATOM   2240  O   HOH E 780       7.009  19.440  56.694  1.00 45.06      W
ATOM   2241  O   HOH E 781      -2.535  -3.002  65.200  1.00 44.49      W
ATOM   2242  O   HOH E 782      29.850  -8.720  55.997  1.00 33.80      W
ATOM   2243  O   HOH E 783      29.002  -1.110  38.096  1.00 49.80      W
ATOM   2244  O   HOH E 784       2.629 -11.502  38.153  1.00 20.48      W
ATOM   2245  O   HOH E 785       8.170  -2.889  59.317  1.00 55.76      W
ATOM   2246  O   HOH E 786      -7.757   7.231  36.343  1.00 44.27      W
ATOM   2247  O   HOH E 787      29.509  41.574  42.391  1.00 30.71      W
ATOM   2248  O   HOH E 788      12.321   5.000  73.438  1.00 39.23      W
ATOM   2249  O   HOH E 789       9.077  -0.805  56.886  1.00 49.68      W
ATOM   2250  O   HOH E 790      20.165   3.781  31.501  1.00 56.66      W
ATOM   2251  O   HOH E 791       9.932   0.809  61.593  1.00 51.39      W
ATOM   2252  O   HOH E 792      -5.760  35.496  52.936  1.00 48.89      W
ATOM   2253  O   HOH E 793       6.379  23.275  56.289  1.00 34.66      W
ATOM   2254  O   HOH E 794      -8.872  27.821  51.823  1.00 45.23      W
ATOM   2255  O   HOH E 795      12.375  13.901  24.850  1.00 36.05      W
ATOM   2256  O   HOH E 796       8.356  10.904  25.421  1.00 36.51      W
ATOM   2257  O   HOH E 797      24.045  36.583  31.107  1.00 27.65      W
ATOM   2258  O   HOH E 798      16.372 -13.823  59.823  1.00 36.61      W
ATOM   2259  O   HOH E 799       3.373  -1.958  66.429  1.00 34.14      W
ATOM   2260  O   HOH E 800      28.182  27.903  50.321  1.00 38.54      W
ATOM   2261  O   HOH E 801      25.336   2.496  55.259  1.00 49.82      W
TER
HETATM 2262 CO  CO  F 400       7.161  20.051  38.857  1.00 17.95      M
TER
END
```

Table 2 - Interactions between the α2 I-domain surface and the triple-helical peptide.

The table shows the co-ordinates of both the receptor and ligand surfaces, defined by identifiable interactions between the two. The interacting residue is indicated as (A) or (M), according to Table 1, representing I-domain or metal ion, respectively, or as (D) or (C), according to Table 1, representing middle or trailing strand, respectively, of the triple-helical peptide. Interacting atoms within the amino acid residue are identified according to Table 1. Hydrophobic interactions, more diffuse in nature are identified by residue number and chain only, not be co-ordinates.

Integrin a2-I domain Co-ordinates (Å)				GFOGER peptide Co-ordinates (Å)			
Residue (chain) Atom	*x*	*y*	*z*	Residue (chain) Atom	*x*	*y*	*z*
Electrostatic Interactions:							
D219 (A) OD1	6.287	22.858	28.292	R12 (D) NH1	1.806	21.563	27.940
D219 (A) OD2	6.053	20.992	29.406	R12 (D) NH2	3.954	21.199	27.207
Co^{2+} (M)	7.161	20.051	38.857	E11 (D) OE1	7.903	21.213	37.093
Hydrogen bonds:							
N154 (A) ND2	11.262	23.084	32.568	O9 (D) OH	14.095	26.856	29.776
N154 (A) C=O	12.723	22.629	37.870	O9 (C) OH	14.426	24.210	39.593
N154 (A) N	10.976	20.327	35.801	E11(D) OE2	5.884	21.318	36.268
Y157 (A) OH	20.258	25.725	43.687	O6 (C) C=O	24.272	24.224	38.878
D219 (A) C=O	5.110	22.362	32.522	R12 (D) N	4.615	25.188	33.098
T221 (A) OH	5.695	19.117	37.506	E11 (D) OE1	7.903	21.213	37.093
H258 (A) NE2	2.099	22.463	35.236	R12 (D) C=O	2.670	25.239	34.916
H258 (A) C=O	-3.002	18.940	36.428	O15 (D) OH	-3.452	20.982	34.490
Hydrophobic Contacts:							
Y157 (A)				F9 (C)			
Q215 (A)				F9 (D)			
N154 (A)				F9 (D)			
L286 (A)				F9 (C)			

Residues E318 (A) and D292 (A) become more exposed upon ligand binding.

Residues L286 (A) and Co^{2+} (M) become exposed and contact ligand.

Claims

1. A method of identifying a potential inhibitor of an I-domain-containing polypeptide, the method comprising the step of employing a three-dimensional structure of the Integrin α2 I-domain as shown in Table 1 to design or select a potential inhibitor.

2. A method of identifying a potential inhibitor according to claim 1, wherein the potential inhibitor is designed or selected to inhibit conformational changes to the C-helix and/or Helix α7 of the Integrin α2 I-domain.

3. A method of identifying a potential inhibitor of an I-domain-containing polypeptide, the method comprising the step of designing or selecting a potential inhibitor that interacts with one or more points in the I-domain crystal structure shown for the I-domain in Table 2.

4. A method of identifying a potential inhibitor of an I-domain-containing polypeptide, the method comprising the step of designing or selecting a potential inhibitor that mimics one or more points in the peptide structure shown for the peptide structure in Table 2.

5. A method of identifying a potential inhibitor according to any one of claims 1 to 4, the method comprising the further steps of:

synthesizing or providing said potential inhibitor; and

testing said potential inhibitor for ability to interact with an I-domain-containing polypeptide.

6. A method of identifying a potential inhibitor according

to claim 5, wherein the testing step includes bringing said potential inhibitor into contact with an I-domain-containing polypeptide to determine the ability of said potential inhibitor to inhibit (i) the ability of the I-domain to interact with collagen or a collagen peptide or other ligand which binds the I-domain, and/or (ii) I-domain or I-domain-containing polypeptide function.

7. A method of identifying a potential inhibitor according to claim 5, wherein testing step includes the sub-steps of:

(i) forming a complex of the I-domain-containing polypeptide and said potential inhibitor ; and

(ii) analysing said complex by X-ray crystallography or NMR spectroscopy to determine the ability of said potential inhibitor to interact with the I-domain-containing polypeptide.

8. A method of identifying a potential inhibitor according to any one of claims 1 to 7, wherein the I-domain-containing polypeptide is an integrin.

9. A method of obtaining a potential inhibitor of an integrin, the method comprising the steps of:

(a) providing a peptide fragment of integrin α2 I-domain, which peptide fragment contains the E318 residue, the D292 residue, or the residues 284-288;

(b) bringing the peptide fragment into contact with a test substance ; and

(c) determining the ability of the peptide fragment to bind with the test substance.

10. A method of obtaining a potential inhibitor according to claim 9, wherein the test substance is an antibody molecule.

11. A method of analysing an I-domain-containing polypeptide complex comprising employing (i) X-ray crystallographic diffraction data from the I-domain-containing polypeptide complex and (ii) atomic coordinate data according to Table 1 to generate a difference Fourier electron density map of the complex.

12. A crystal of α2 I-domain complex having a space group $P2_12_12_1$, and unit cell dimensions of a = 42.0 Å, b = 48.4 Å, and c = 114.5 Å.

13. A crystal of α2 I-domain complex having the three dimensional atomic coordinates of Table 1.

14. A computer system, intended to generate structures and/or perform rational drug design for I-domain-containing polypeptides or I-domain-containing polypeptide complexes, the system containing atomic coordinate data according to Table 1 or Table 2.

15. Computer readable media for use in the computer system of claim 14, having atomic coordinate data according to Table 1 or Table 2 recorded thereon.

16. An inhibitor of an I-domain-containing polypeptide which is identified or obtained by any one of methods 1 to 10.

17. The inhibitor of claim 16 for treatment of a disorder or disease.

18. Use of the inhibitor of claim 16 in the manufacture of a pharmaceutical composition for the treatment of a disorder or disease.

19. A method of making a pharmaceutical composition comprising admixing the inhibitor of claim 16 with a pharmaceutically acceptable excipient, vehicle or carrier.

20. A method of treating a disease or disorder in which an I-domain-containing polypeptide has a role, comprising administering an effective amount of an inhibitor of the I-domain-containing polypeptide to an individual, the inhibitor being identified or obtained by any one of methods 1 to 10.

Figure 1

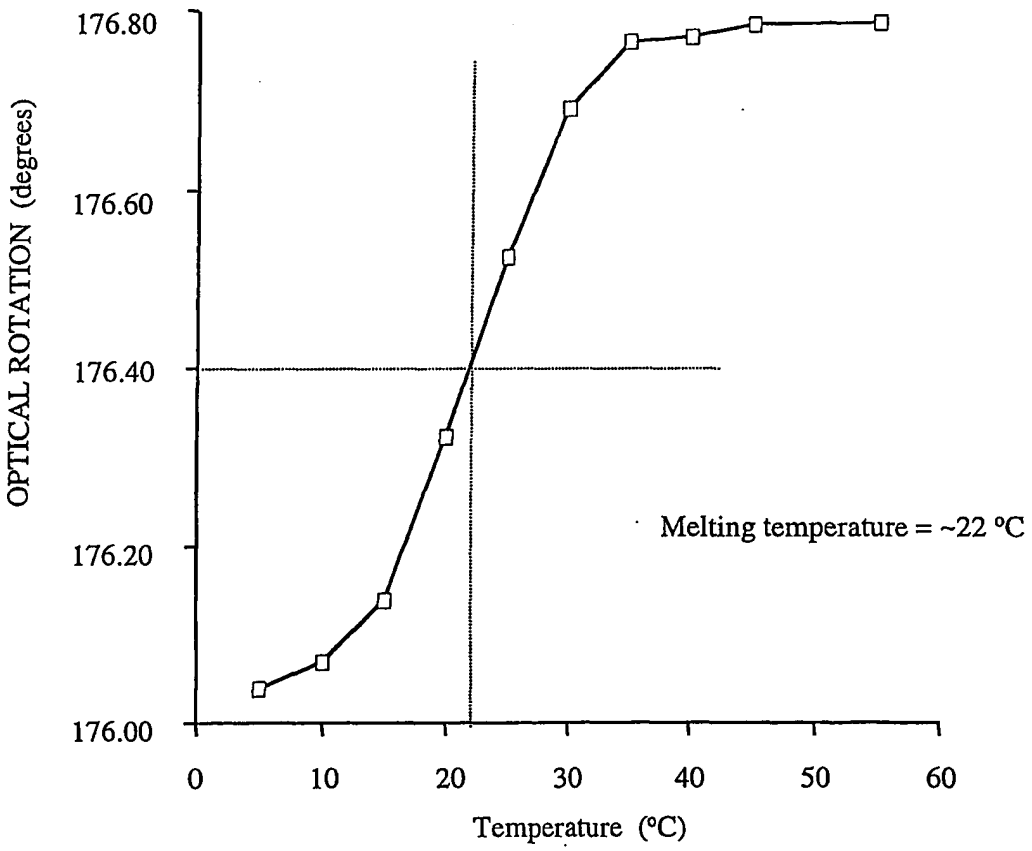

176.80
176.60
176.40
176.20
176.00
OPTICAL ROTATION (degrees)
0
10
20
30
40
50
60
Temperature (°C)
Melting temperature = ~22 °C

Figure 2

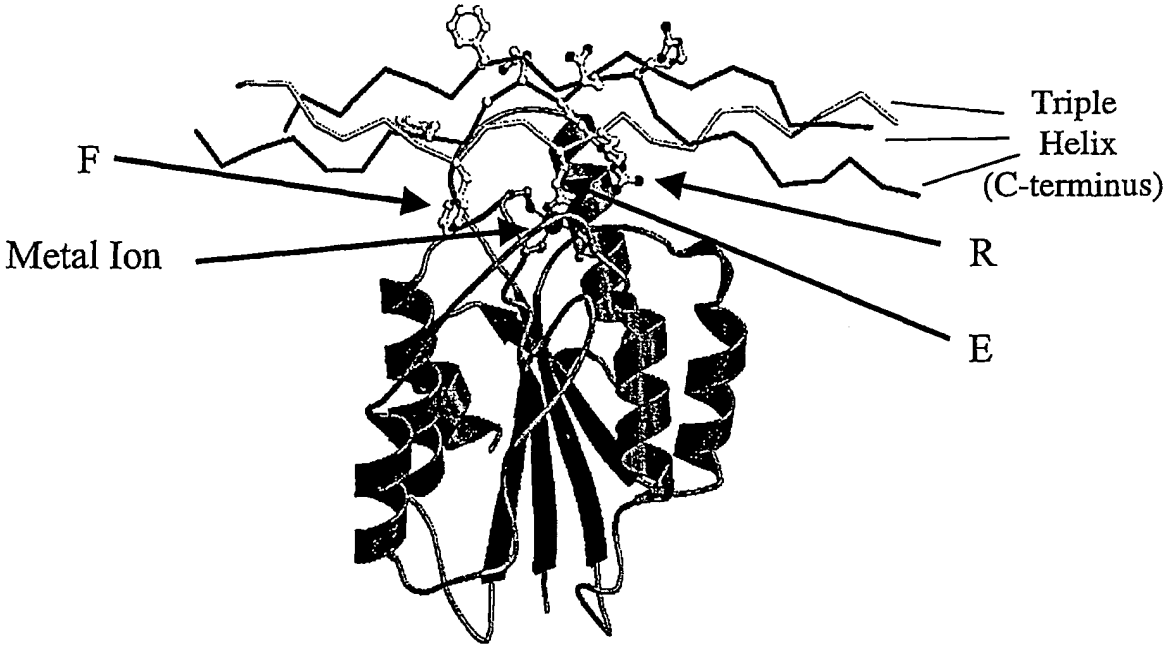
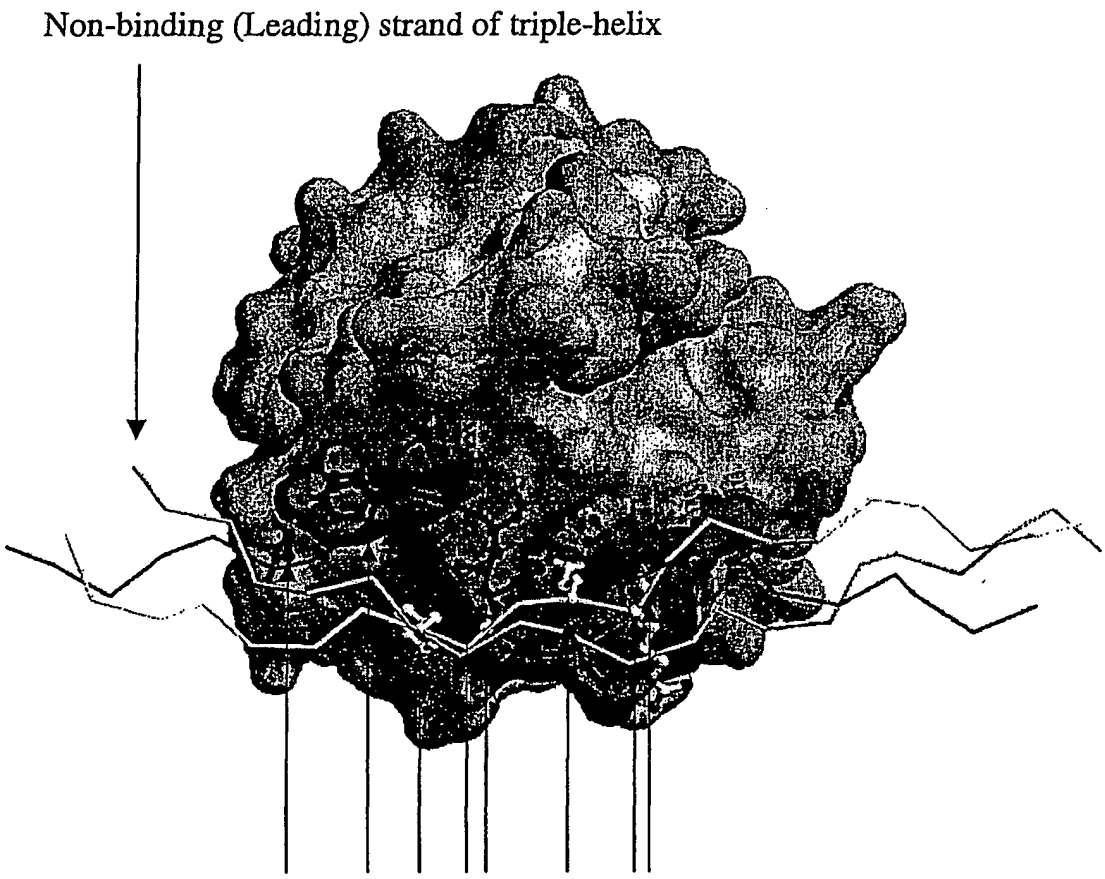


Figure 3



Triple-helix Middle and Trailing strand interactions with I-domain

Figure 4

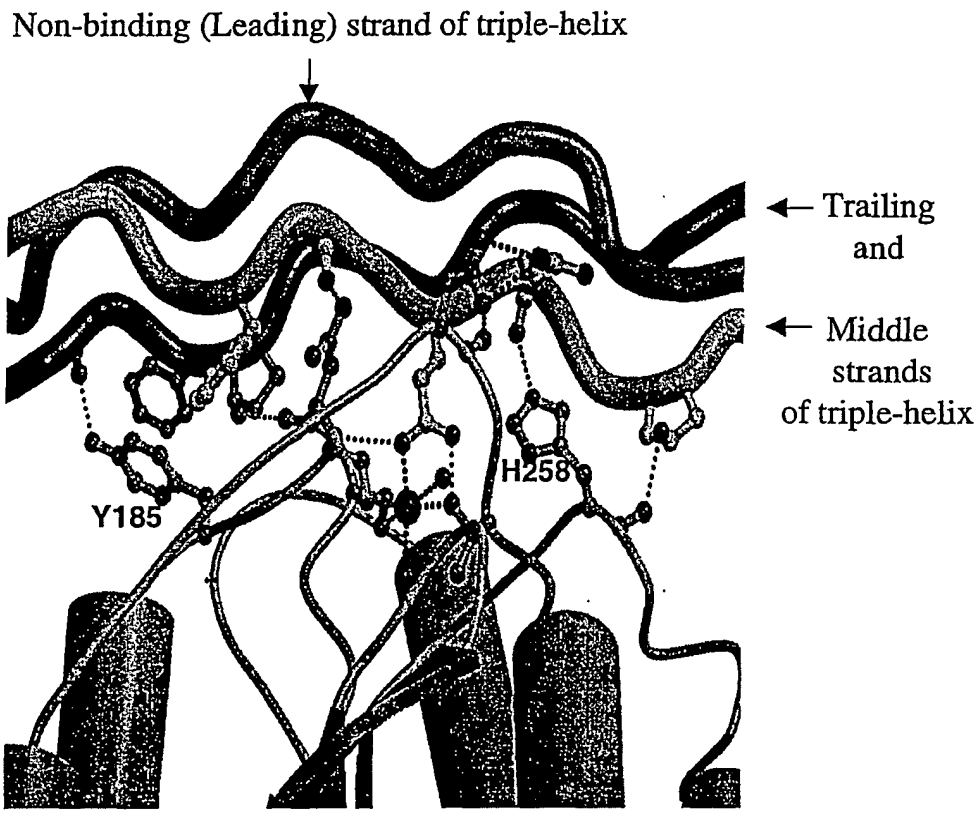

Non-binding (Leading) strand of triple-helix
Trailing and
Middle strands of triple-helix
H258
Y185

Figure 5

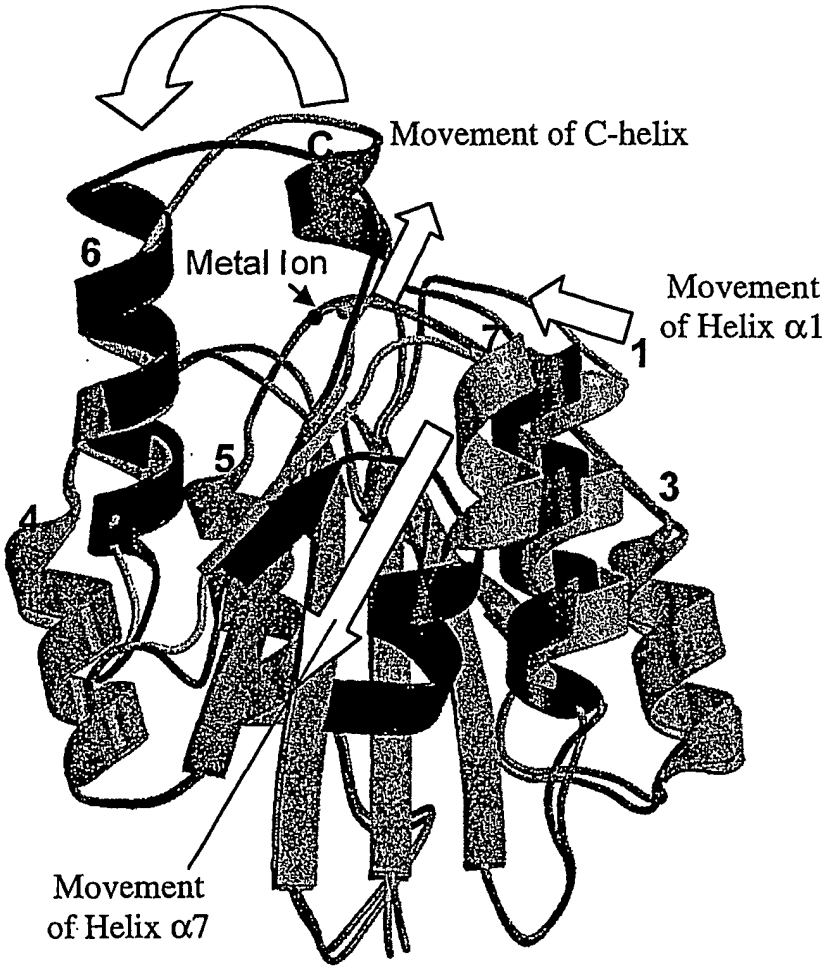
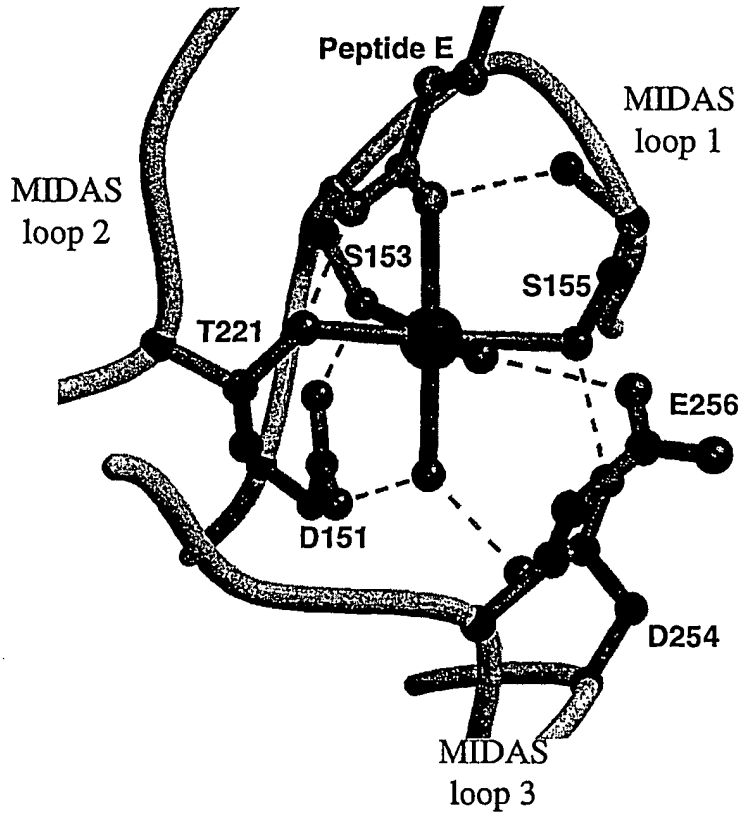

Movement of C-helix
C
6
Metal Ion
Movement
of Helix α1
1
5
3
4
Movement
of Helix α7

Figure 6


Peptide E
MIDAS
loop 1
MIDAS
loop 2
S153
S155
T221
E256
D151
D254
MIDAS
loop 3